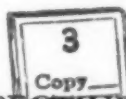


# SCIENCE

NOVEMBER 3, 1950



INSTRUMENTATION IN PERSPECTIVE

W. A. WILDHACK

SECTIONING OF TISSUE  
FOR ELECTRON MICROSCOPY  
JAMES HILLIER AND MARK E. GETTNER

TECHNICAL PAPERS

COMMENTS AND COMMUNICATIONS

BOOK REVIEWS

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NEWS AND NOTES



COMPLETE TABLE OF CONTENTS ON PAGE 3

VOLUME 112, NUMBER 2914

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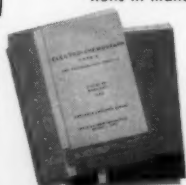
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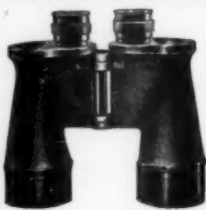
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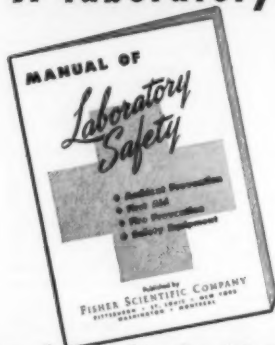
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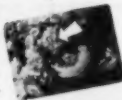
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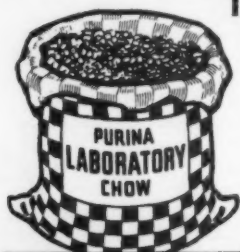
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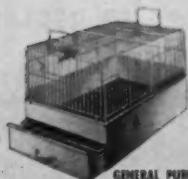
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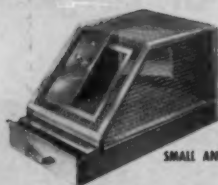




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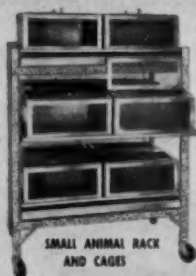
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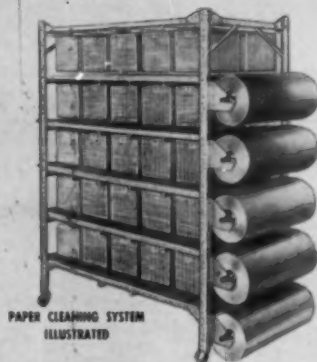
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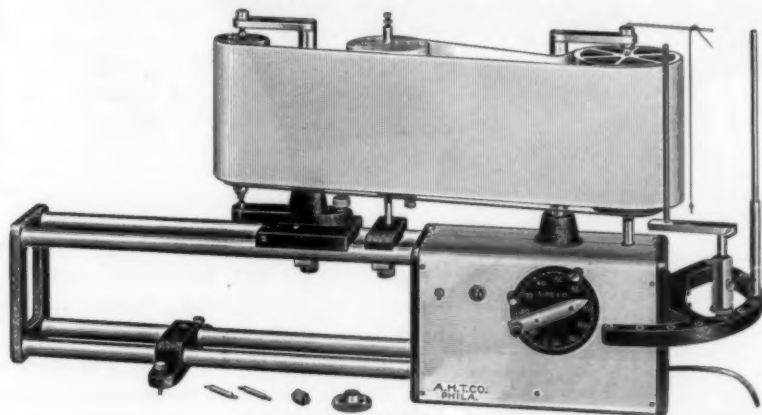
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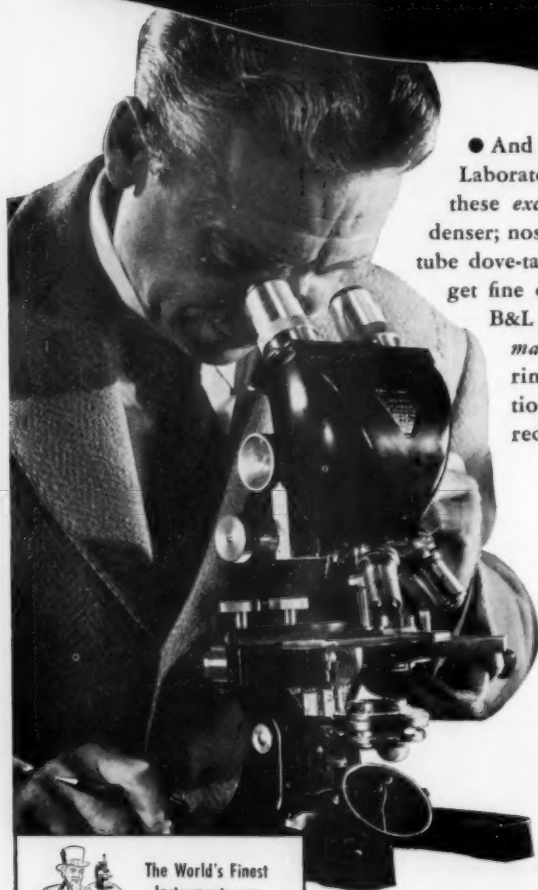
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# Instrumentation in Perspective

W. A. Wildhack

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THE TIME IS LONG SINCE PAST when any one man could know all contemporary science, and the time is almost past when a specialist in any one field can maintain acquaintance with even the high spots of many other fields. It might be assumed that the knowledge and interest of the specialist concerning the instruments and techniques used in building the structures of other sciences would be even more casual, fragmentary, and remote than his knowledge and interest concerning the final conclusions reached by those sciences, but this is not necessarily so. It is becoming generally recognized even by the most academic scientists, who are noting the more alert practices of their industrial colleagues, that many instruments and techniques developed for one particular field will find applications of equal or even greater importance in other quite unrelated fields. The astute experimentalist has therefore learned to keep his eyes open for advances in instrumentation wherever they may occur.

The remarkable development of measuring devices and techniques in the past two decades, following the logical implications of the concept of mass production, and the imperatives of automatic control of continuous processes, have supplied the scientific worker also with off-the-shelf equipment for measurement and control beyond the wildest dreams of an earlier generation, which had to spend much of its time in the design, fabrication, and repair of relatively crude measuring devices. Some understanding of the great variety of available instruments is essential to the modern scientist, not only to save his own time—for better concentration on his own particular research—but also to suggest new and fruitful lines of approach to his goals. Thus there is a very real and live interest in instrumentation on the part of scientists generally.

The scope and complexity of science and of technology are reflected in the overlapping of the various subjects that comprise the "field of instrumentation," making it difficult for the investigator to keep abreast of all the developments in instrumentation that are pertinent to his work, or to solve unaided the instrument problems incident to his goal, if he is at the

same time to maintain a mastery in his own area of specialization. Thus it happens that experts in one or more of the various *types* of instruments have been more and more frequently called upon for advice and consultation, and the growing demand has encouraged a number of engineers and scientists to specialize in this phase of scientific work. In this work they have gone beyond familiarity with *instruments* and have concerned themselves also with the problems incident to the broader phases of instrumentation. They have familiarized themselves with the relationship between classes of instruments, the problems common to the design and application of all types of instruments, the analysis of instrument systems, and the theory and practice of applying measurement to the broad field of automatic control. In short, they have evolved the Science of Instrumentation. The specialists in this new science make their chief goal the improvement in the means whereby others may attain the ends of other fields of experimental science and technology.

The growth of this kind of specialization proceeded initially, and most rapidly, in industry. Chemical, electrical, and mechanical engineers acquired the title of "Instrument Engineers" and accepted the responsibility for selection, procurement, adaptation, and, frequently, for design and development of instruments for use in plant processes, as well as in plant laboratories.

A parallel evolution of specialists occurred in the instrument manufacturing industry, where engineers and physicists were essential not only for development design, but also for application (or sales) engineering. The intimate knowledge of industrial measurement problems gained by technically competent field representatives, working with the plant engineer or laboratory scientist to define needs, and with the manufacturers' design engineers to achieve a usable answer to those needs, has aided greatly in the rapid invention of practical, well-designed, and reliable devices for measurements of all types.

It is through academic research that fundamental problems have traditionally been solved, and the solutions first applied to new methods of measurement.

This continues, but usually the academic specialist in pure science is only secondarily concerned with exploring all the implications and applications of his discoveries in the broad field of measurement, whereas the engineer is generally concerned with measurements only in his particular field. Not until the past decade has it been widely recognized that the progress of science, as well as of technology, can be greatly accelerated by focusing specifically on the wider exploitation of existing techniques of measurement and on the improvement and development of new instruments and methods for measurement and control.

With a few noteworthy exceptions, university educators have been slow to provide their graduates with specific training relating to instruments, control systems, or the theory of measurement generally. Specialized education in the field of instrumentation, *per se*, has been primarily a matter of self-education, at least until recently.<sup>1</sup>

However, for those who sought familiarity with instruments and instrumentation there has always been a rich field of reference material available in all the sciences. For nearly twenty-five years two American periodicals have been devoted to the dissemination of information on instruments: *The Review of Scientific Instruments*, limited largely to research papers, and *Instruments*, the magazine of measurement and control, limited largely to descriptions of industrial instruments. Both these magazines have been effective media, not only for the dissemination of information on specific instruments, but also for the "propagation of the gospel" of increased productivity in science and industry through measurement and control. M. F. Behar, longtime editor of *Instruments*, was an early and leading proponent of this gospel and an exponent of the science of instrumentation, and this magazine is notable for its editorial emphasis on the important role of instrumentation and its even greater potentialities.

Abroad, the British *Journal of Scientific Instruments*, the German *Zeitschrift für Instrumentenkunde* and *Archiv für technischen Messen*, and the French *Revue de Metrologie* were the primary prewar journals dealing with instruments. Both in this country and abroad, however, many of the basic papers dealing

with fundamentals of measurement, automatic control, transmission and recording of data, design of fine mechanisms, and development of general-purpose instruments continue to appear in other professional journals. The American Society of Mechanical Engineers has a notable record in this respect; its Industrial and Regulators Division was created to give greater recognition to this phase of mechanical engineering, and many significant papers have appeared in its publications. The American Institute of Electrical Engineers likewise has an active committee on instruments and measurements; and many of the activities of the Institute of Radio Engineers, as well as the papers in its journal, relate to instruments and measurements.

The *Proceedings of the Royal Society*, the *Philosophical Magazine*, the *Journal of the Optical Society of America*, *Industrial and Engineering Chemistry*, to cite only a few examples here and abroad, are fruitful references for papers on the general aspects of instrumentation. Various sectors of instrumentation are specifically encompassed and cultivated by other societies, such as American Microscopical Society, American Society for X-Ray Diffraction, the Electron Microscope Society, the Society for Experimental Stress Analysis, etc. One organization, the Instrument Society of America, founded in 1945 and having now about 4,000 members, devotes itself to the broad aspects of the art and science of instrumentation. The AAAS-Gordon Research Conferences sponsor a week-long session on instrumentation related to chemistry each year. The action of the editors of *SCIENCE* in devoting a special issue every year to instrumentation, indicates the growing recognition of the importance of instrumentation to science.

Like all of "science," the "science of instrumentation" may be recognized without being very exactly defined. It is not unique in this respect; most other branches of science are fuzzy at the edges; but, with no attempt at precision, we may characterize the field of instrumentation, first, by its relation to the other sciences; second, by its content; and, third, by its goals. In relation to other sciences, instrumentation is a horizontal field encompassing segments of practically all of them. This is well illustrated in an article by Waterfall and Hutchisson on "Organization of Physics in America" (1). In a chart showing the various vertical divisions of science, such as physics, chemistry, geology, biology, etc., and even their subdivisions, such as mechanics, sound, heat, light, metallurgy, surgery, physiology, etc., each field broken down by content, including one area called Instrumentation, the general field is presented as a horizontal division across all the sciences. This appears to be a useful and valid concept, and has led to the characterization

<sup>1</sup> The Massachusetts Institute of Technology and Columbia University have long offered instruction in automatic control, servomechanisms, instrument theory, etc. Many physics departments have given traditional courses in "physical measurements," and many engineering and science courses include much work on certain classes or types of instruments; but courses dealing broadly with the study of instruments are only now being added to university curricula. In this connection, a conference on "Instrumentation and the University," sponsored by the Instrument Society of America in 1945, helped to focus attention on the need for such training, with the result that many more institutions have since introduced courses in instrumentation.

of instrumentation as the common denominator of the sciences (2).

Just as the whole is often greater than the sum of its parts, so is the science of instrumentation greater than the sum of the individual phases of instrumentation that are inherent in the fields, for instance, of electricity, mechanics, electronics, optics, etc. It includes, besides the science of instrument design and application, the broad principles and general theories of measurement and control, and the operational analysis of the various steps in the handling and use of measurement data.

In the article by Condon (3), in the Annual Instruments Issue of SCIENCE on "Is There a Science of Instrumentation?" the question raised by the title was answered in the affirmative, with emphasis on the common elements in the problems, devices, and methods of measurement.

In another recent article, Trimmer (4) compares several views of instrumentation, without quite deciding whether it is a part of the newly introduced (and not-yet-quite-accepted) science of cybernetics named by Wiener. Wiener's book (5), subtitled *Control and Communication in the Animal and the Machine*, emphasizes the similarities between the methods of communications engineering and the physiological transmission of information by nerve action, and the probable benefits to each field that will result from intermixing the concepts and methods of each. It is certainly true that the problems of control are essentially the same for any living organism as for an automatic control instrument or instrument system. In both the animal and the instrument, stable control implies a "feedback" of output into the sensing element, and the principles of automatic control must be equally applicable to both. Having defined instrumentation as "the science of measurement and control," one might (with the permission of the communications engineers) include communication devices and theory, as well as automatic control. The domain of cybernetics then would appear to be instrumentation in the fields of psychology and physiology. However, we may leave to the future the decision as to whether cybernetics shall become an inclusive science, and, if so, whether instrumentation is a part of cybernetics or vice versa.

There is one other branch of science with which instrumentation is closely allied—so closely in fact, that instrumentation may be called the offspring of metrology. Some distinction may be made, however, between these fields, in the light of their differing emphasis. Metrology concerns itself not only with the devices of measurement but also with the carrying out of measurements and the compilation of data. Instrumentation puts prime emphasis on the develop-

ment and application of the devices and techniques of measurement, and not so much on the continued utilization of the instrument for measuring purposes, or on the results of the measurements. Further, instrumentation apparently includes in its domain the important and expanding field of automatic control, and the theory of feedback of an instrument output to amplify that output by regenerative action, or to stabilize the output by negative reaction with the physical magnitude to be controlled. But it is fruitless to attempt too exact a definition of a subject that is so interwoven in others, and that is unique primarily on that account. Those parts of science generally which deal with instruments, with measurements, and with control combine to form the core of the science of instrumentation.

Looking broadly at all types of measurement, it is easy to see that there are several very distinct and separate parts, steps, or links involved in the complete measuring and control process. It is also easy to recognize that a number of common elements enter into the problems associated with all types of measurement.

1. First in the chain is, of course, *detection or response*. There are literally thousands of devices now available that detect or respond to some property, condition, or variation related to measurable magnitudes. Such "condition-responsive," detecting, or signal-generating elements, as they are variously called, have the common function of responding to the thing to be measured, with a resulting change in some other thing that can be measured. The generic term for such devices is *transducer*, which may, in its broadest sense, be defined as a device that responds to one physical entity, or change therein, by producing a change of some other condition, factor, or entity. A simple example is a mercury-in-glass thermometer, which responds to changes in condition—temperature—by changes in volume. To cite another illustration from the outer regions of our perhaps slightly stretched definition, a photographic plate that responds to light exposure by a change in the developable property of the emulsion may also constitute a transducer.

2. The second element is *transmission*, if the information is to be dealt with at a location remote from the point of measurement. A simple variant of the mercury-in-glass thermometer has an extremely long stem so that the movement of mercury in the capillary will be transmitted the requisite distance. Alternatively, the expansion of the mercury may change the amount of the metal in a stem surrounded by a coil, so that the electrical impedance of the circuit is changed; this change may be indicated at a distance. Or the expansion may move a flexible member to in-

terfere with the flow of gas through an orifice, and the resulting change in pressure may be transmitted through a pneumatic circuit.

In order to have a signal of sufficient strength for transmitting over long distances, or to operate indicating or recording devices, it is often necessary to add another step to the measurement process—namely, amplification. Any of these types of output may be further transformed into radio signals for still further transmission, leading into the entire field of radio telemetering.

3. *Indication* is a third factor which, in the primitive stages of measurement, was the end result. The pressure gauge, the electric meter, the visible fluid in the thermometer stem, are simple and familiar examples. The impact of psychology, physiology, and operational analysis may radically change the appearance and operation of the conventional needle-and-scale-type of indicating instrument. Digital representation of the measurement will probably be more and more frequently employed, leading to indicators like the ordinary automobile mileage indicator. The cathode-ray tube may be mentioned as a very convenient and versatile indicator wherein the scales and method of presentation may be varied at will.

4. Whether or not the result of the measurement is to be shown on an indicator, *recording* is often desirable, to make a temporary or permanent record of the measurement as a function of time or of some other parameter. The photographic recording of light beams reflected by moving coil galvanometers is one method of keeping track of rapidly changing measurements. The moving pen actuated by the measuring instrument or by a repeater, recording on circular or strip charts, is the commonest method of making records. A variety of repeater mechanisms has been developed for accurately, rapidly, and exactly positioning the pen in response to very slight signals, so that multirange recorders are now to be found in all laboratories. The recent development of means for storing information on magnetic wire or tape, which can eventually be erased and used again, has opened up new possibilities in this field.

5. When measurement information is obtained, transmitted, and indicated or recorded, it is logical to add *control* to the duties of the instrument, so that it may carry out the task of negotiating or doing those things the human operator would do if he noted the indication and followed the logical consequences dictated by the measurement. The output that operates the indicator or recorder is also compared with what is desired, and the difference between the actual and the desired, constituting an *error signal*, serves to set other devices in motion to change the thing which was measured. The simple household thermostat

turns off the furnace when the temperature attains a certain value and turns it on again when the temperature falls below another certain value. The complex antiaircraft fire controller combines various measuring devices to determine height, range, direction, and velocity, and rate of change of course of the aircraft, computes the trajectory, allows for the characteristics and location of the gun, and sets in motion the controls to point the gun in the correct direction. Between these examples are a host of existing and potential devices and problems for automatic control.

6. Of a somewhat different character from the control procedure, the instrumental function of *data reduction and analysis* is also derived from the measuring action of instruments, through extension of the function to perform those steps that the human operator would take from logical consideration of the implications of measurement. An example is in the target scoring devices developed during the last war for gunnery training. Measurements were made of the direction in which the trainee pointed the gun when firing and were automatically correlated with the position of the simulated moving target on the screen. When the measurement fell within the moving range, a "hit" was automatically recorded and the number of hits totaled. In a more sophisticated device the average angle-of-miss could be measured and recorded for better training. In some cosmic ray studies the passage of a ray is in itself not a noteworthy event, but the statistical variation of the type and energy of the ray, perhaps only in its correlation with other variables, is significant. Here the primary measurements may be considerably distorted and simplified to reduce the problem of correlation to its simplest essentials. In this direction the development of devices for the automatic drawing of conclusions from data automatically sifted, sorted, reduced, and analyzed, is only in its infancy.

Since instruments are material entities, they are subject to ills arising from the idiosyncrasies of the material of which they are made, as well as those arising from the inevitable application of the third law of thermodynamics. Many of these elements may be grouped under one general heading as affecting accuracy: response characteristics, hysteresis, drift, repeatability, effect of overload. These effects may have a multiplicity of causes, such as friction and looseness in bearings, the misreading or dislocation of the pointer, the elastic defects in sensitive elements or supporting structures, changes in electrical, optical, or other properties of materials on which the performance depends, leakages, or instability of amplifiers, resistors, etc. Another class of problems relates not so much to accuracy as to physical characteristics desirable in instruments—compactness, portability,



ruggedness, insensitivity to shocks and extremes of temperature, pressure, humidity, etc. Inasmuch as each successive factor in the instrument control cycle has its own shortcomings and defects, the struggle to maintain accuracy, reliability, repeatability, ruggedness, etc., is increased almost exponentially with the number of elements or links in the system. The many continuing problems, together with the stream of improvements being devised, and new materials being employed, promise a busy and fruitful future for the field of instrument engineering.

It would be an interesting but endless task to enumerate possible and expected developments in the many types and classes of instruments and control devices for general and special purposes. In a brief compass, only some of the general lines in which progress appears in the making may be listed.

1. It is easy to foresee an increased recognition for the science of instrumentation. Except for atomic energy, the development and application of instrumentation probably have greater potential material significance for our age and our civilization than any other factor on the contemporary scene. This seems valid militarily, industrially, and scientifically.

2. We may expect an accelerated trend toward educating scientists and technologists in instruments and instrumentation, so that within a few years accredited colleges of science and technology will have required survey courses in instrumentation for all undergraduates, as well as specialized courses on instruments in the specialized fields of engineering and science.

3. The foregoing factors will accelerate the present rapid rate of improvement in devices and materials, in methods and techniques for recording, transmission, especially telemetering, and in control systems, and in data reduction and analysis. Many of these improvements will probably result from intensive studies of the general factors in the control cycle which are entirely independent of the particular magnitude to be measured.

4. Extensive improvement in the classification of

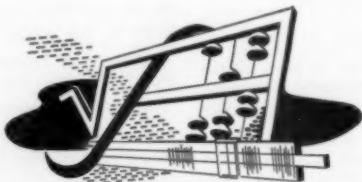
fields of instrumentation, of instruments, the uses of instruments, and the problems associated with instrument design and utilization is inevitable. More effective indexing, abstracting, and publication of information are assured in this field. Systematic surveys will be made of classes of instruments to determine their limitations and their potentialities and to extend their usefulness into other fields of measurement beyond those now being explored. Similar surveys of classes of measurement will help to indicate weaknesses in the design, construction, or operating principles of available instruments, and thus lead to intensive efforts for their improvement. Furthermore, systematic surveys of all physical principles useful for sensing, amplifying, recording, or for any other step in the measurement cycle will undoubtedly lead to a considerable increase in the already rich field of possibilities available to the instrument designer.

5. One may confidently predict also an increasing growth in the instrument industry, as both science and technology become even more dependent on large numbers of a large variety of instruments.

6. Finally, one may confidently anticipate an acceleration and continuation of the fruitful cross-fertilization of the various sciences that results from the development of instruments. One need only list a few of the instrumentally based fields that have, in the past decade, grown far beyond their modest beginnings to realize that this is only a start: spectrophotometry, mass spectrometry, microwave spectrometry, nuclear resonance techniques, radioactivity measurements, analogue computers and simulators, high-speed digital computers, magnetic recording, ultrasonics. Who can say what new instruments, and from them what new sciences, 1960 will see?

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# Sectioning of Tissue for Electron Microscopy<sup>1, 2</sup>

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PEASE AND BAKER (3) made a major contribution to the use of the electron microscope when they showed that it is possible to cut sufficiently thin sections of tissue by relatively simple modifications of conventional microtomes and techniques. The early results obtained by these workers and by others who have followed their technique, or modifications of it, have shown, however, large-scale and obvious artifacts that detract considerably from their value to the cytologists and pathologists who might ultimately be interested. Since these artifacts were somewhat greater than are normally encountered in conventional light microscopic techniques, it could be anticipated that they arose either in the ultra-thin sectioning or in the subsequent handling of the specimens.

## IMPROVEMENTS IN ULTRA-THIN SECTIONING OF TISSUE

In the present work an analysis was made of these aspects of the Pease and Baker technique in order to identify and eliminate the sources of the artifacts. The results of the analysis are presented briefly in the following pages, but a more detailed report will be presented elsewhere (2).

Since the aim of the present research was to study the cutting and mounting of the sections, an attempt was made to eliminate the variables involved in the selection, fixation, and embedding of the tissue by studying a single set of blocks originating from one piece of tissue. As the best micrographs in the literature appeared to be those in Pease and Baker's original work, the same type of specimen and identical embedding techniques were adopted. The specimens<sup>3</sup> consisted of a normal mouse liver perfused for

24 hours with 1 percent osmium tetroxide in physiological saline. It was then cut into pieces a few millimeters on the side. These were dehydrated through alcohol, embedded in 12 percent collodion, hardened with chloroform, cut into 1-mm cubes, mounted and impregnated with 60° paraffin. Since all the steps were carried out simultaneously, the only likely variation would result from the low penetrating power of the osmium. The results indicated that the fixation was quite uniform. Having uniform blocks eliminates a large number of variables and greatly simplifies the sectioning problem, which can then be divided into three distinctly separate steps to be considered independently. These are (1) the advancing of the block by uniform and specified amounts, (2) the cutting of the sections, and (3) the mounting of the sections.

1. *Block advance.* In the Spencer rotary microtome, unmodified except for the changed angle of the inclined plane, the variations in block advance had a mean value between 0.1  $\mu$  and 0.2  $\mu$ . These variations were found to be due to external vibrations, irregularities introduced by manual operation, static friction in the screw and associated parts, and static friction in the horizontal slides. To eliminate these effects, the following changes were made: (a) A motor drive with a vibration-free coupling was added. (b) The unit advance was set at 0.02  $\mu$ , so that the motions in the screw, screw bearings, and pointer bearings were all large for normal section thicknesses of 0.2  $\mu$ . This also reduced the effect of inaccuracies in the screw. (c) Ninety percent of the weight of the inclined plane and the attached block support was removed from the horizontal slides by means of a leaf spring. In the microtome used, there is a horizontal excursion of the block amounting to 300  $\mu$  in each cycle, which removes most of the static friction from the horizontal slide system. The last modification reduces the static friction that enters when the horizontal movement of the block stops at each end of the cutting cycle. As a result of these modifications, the variations in the magnitude of the advance have been reduced to less than 0.01  $\mu$ .

Thermal drifting of the block introduces some error of calibration but does not produce variations in thick-

<sup>1</sup> This work was sponsored, in part, jointly by the Office of Naval Research under Contract No. N6-ori-99 Task Order I and the Atomic Energy Commission, and, in part, by the Lillian Babbitt Hyde Foundation. The electron microscope used was supplied through the kindness of New York University.

<sup>2</sup> Based on a paper presented at the Washington, D. C., meeting of the Electron Microscope Society of America, October, 1949 (Abstracts 13 and 14, *J. App. Phys.*, 1950, **21**, 67).

<sup>3</sup> The authors wish to thank J. J. Bieseke and J. A. Jacques for providing carefully prepared specimens and for their many helpful discussions.

ness when the microtome is motor-driven. The change in calibration was found to be negligible if lights and drafts were kept from the instrument. To check for thermal drifting, it has been found most convenient to retract the block a known number of cycles while the sections are being cut, and to observe whether the first new cut is made on the correct cycle. By noting the error and its polarity, it is a simple matter to compute the true amount of the advance. It is now considered that the thickness of the layer removed from the block is known to within 10 percent.

**2. Cutting.** Very little reliable information has yet been obtained with regard to the optimum values of the various parameters that concern the actual cutting of the block. In the work presented here, commercially sharpened knives were used and proved reasonably satisfactory for  $0.2\ \mu$  sections, though a smaller number of localized defects in the edges would be desirable. Contrary to the experience of Pease and Baker (1), the cutting was found to be very insensitive to the angular setting of the knife. This may be due to the use of the liquid-reservoir method of collecting specimens. The remaining aspects of the cutting that were studied are described below and in the more detailed papers (3).

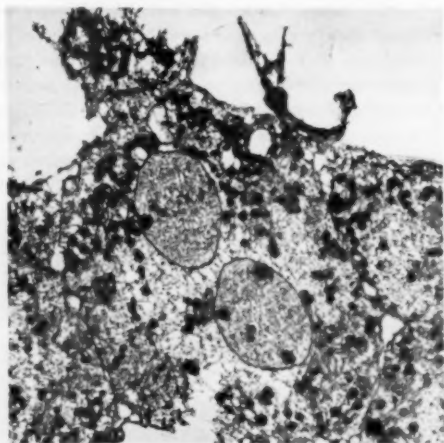


FIG. 1. Normal mouse liver fixed by perfusion with 1% osmium tetroxide in physiological saline. Section thickness  $0.2\ \mu$ . Embedding was completely removed and replaced by thin collodion membrane for support. Note general distortion of cytoplasmic components leaving open network structure. Approximately  $\times 2500$ .

**3. Mounting sections.** In the early work, the most generally used method of mounting sections after cutting was to remove the embedding materials with appropriate solvents and to replace them with a very dilute collodion solution that acted as a support for the dried tissue sections. A study of a few serial

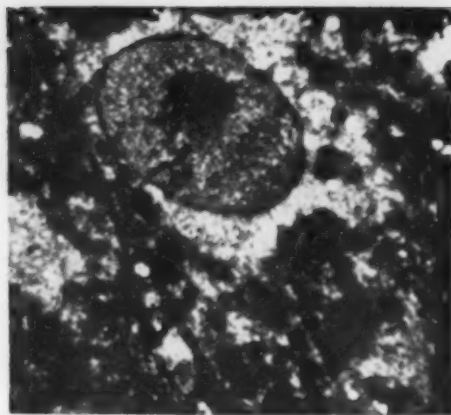


FIG. 2. Same specimen and section thickness. In this case embedding was completely removed and replaced with sufficient collodion to provide film slightly thicker than section. The surface tension effects producing the distortions in Fig. 1 are now absent. However, comparison with Fig. 3, B shows that finer particles have migrated and attached themselves to the coarser structures. Note increased thickness of the cell and nuclear membranes, and general matting of the cytoplasmic structures. Approximately  $\times 5000$ .

sections quickly revealed that the surface forces acting on the tissue in this method produced a typical distortion that was very often large-scale and was primarily responsible for the defects observed in the early work (Fig. 1). This was modified by replacing the embedding material with an amount of collodion that would dry to a film somewhat thicker than the section. This eliminated the distortions caused by surface forces, but greatly reduced the contrast obtainable in the electron micrographs. Contrast was improved by the use of longer focal length objectives with small limiting apertures ( $50\ \mu$  diameter). However, successive serial sections still revealed changes that appeared to be due to a migration of the unsupported smaller structures during the dissolving of the embedding medium (cf. Figs. 2 and 3B). This discovery led to the simplest and most effective of all the techniques, namely, giving the sections no treatment whatever.

The present technique consists of mounting a 200A clear collodion membrane on a square inch or more of 200-mesh copper screen (etched to give more than 50 percent open area) and, after drying, using appropriately sized pieces of it to lift the sections directly from the liquid in the reservoir. The extra collodion membrane serves to anchor the sections to the screen.

With these techniques a large number of very consistent micrographs of the mouse liver have been obtained. Fig. 3 is a typical example. Some artifacts are still introduced, consisting mainly of "knife

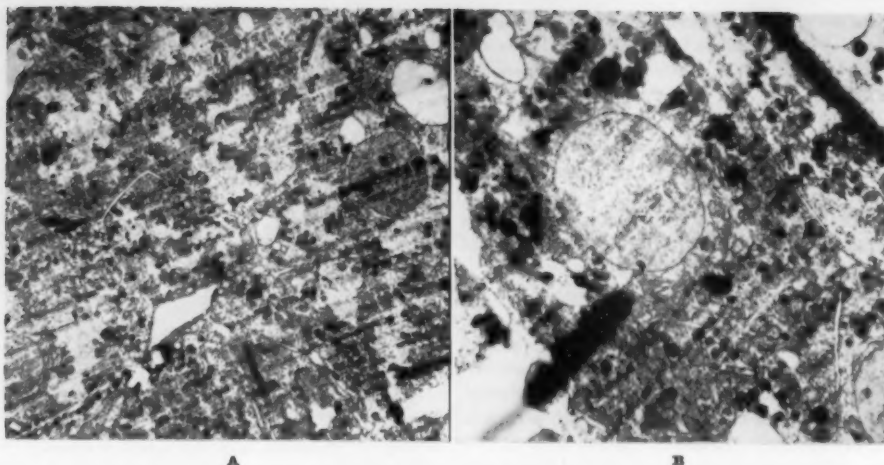


FIG. 3. A, same specimen and section thickness. In this case the section was mounted without treatment. "Knife marks" and occasional slight folds represent the only artifacts of sectioning in this relatively large field. Approximately  $\times 1400$ . B, same specimen, section thickness, and treatment as in A. Note extreme fineness of nuclear membrane in comparison with Fig. 2. Note also individual cell membranes for adjacent cells and multitude of cytoplasmic structures. The heavy line at the top right-hand corner is a fold. The more diffuse broad band in the lower left-hand corner is a defect introduced by the dense granule at the inner end. Approximately  $\times 3100$ .

marks," occasional folds, and local deformations caused by different cutting properties of parts of the tissue, especially near large blood vessels. Most of the artifacts do not interfere with the correct interpretation of the images. However, there is, as yet, no control on the artifacts introduced by the fixation and embedding of the tissue. Preliminary trials of the technique on other material have given varying degrees of success. They indicate the need to adjust the embedding to the hardness of the tissue being cut, and to employ sharper knives.

#### SERIAL SECTIONS

When a Spencer rotary microtome (No. 820) is modified according to the method described by Pease and Baker (3) to cut sections of the thickness suitable for examination by means of the electron microscope, serial sections cannot be cut in the conventional way. However, the necessity of having serial sections is apparent when one considers that more than 100 sections are required to survey a single cell. Furthermore, serial sections provide the most direct indication of the artifacts introduced by the sectioning and mounting procedures.

The failure of the Pease and Baker technique to provide serial sections is a result of the extreme flexibility of the thin sections, which allows them to be rolled and folded by the slightest resistance encountered after being cut. Subsequent spreading and flattening of a number of consecutive sections on a liquid

surface are exceedingly difficult, if not impossible, and are further obstructed by the destruction and adhesions produced by removing the dry group of sections from the edge of the blade. In the present work these difficulties have been largely overcome by bringing a liquid surface to the cutting edge of the knife, and by allowing the sections to float to the surface of the liquid as they are cut. When the surface tension and level of the liquid are adjusted properly, the sections

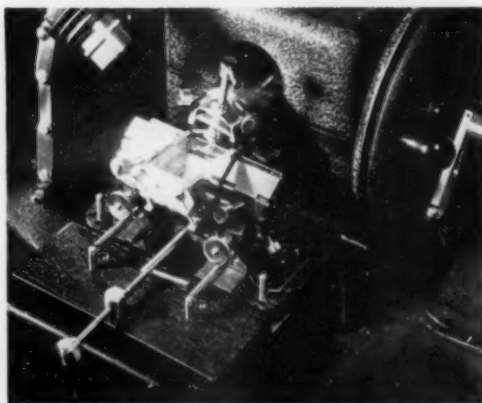


FIG. 4. Photograph of the liquid reservoir as attached for actual cutting. Also shown is a modification of the microtome, which permits a more critical initial adjustment of the knife. The illuminator shown in this photograph was found to introduce intolerable thermal drifting and is no longer used.

are kept full-extended, and long ribbons of sections are obtained ready for mounting (2).

The liquid is contained in a reservoir, which is clamped on the knife between its supports (Fig. 4). It consists of a trough machined from aluminum. The knife acts as the end wall of the reservoir, the seal between it and the trough being provided by a gasket fitted into a groove around the end of the trough. Two levers with hooked ends that pass under the knife, and two screws acting on the opposite ends of the levers, comprise the clamping mechanism. It is obvious that the reservoir must extend somewhat above the edge of the knife, and that the seal between the reservoir and the knife must reach the edge. As might be expected, this leads to some impairment of the edge at the point where the gasket is pressed against it, but the defect introduced is slight and is removed by normal sharpening.

The specimens used in the present work were doubly embedded in collodion and paraffin. Forty percent alcohol proved to be the most generally satisfactory liquid, though it was found desirable in many cases to adjust the concentration. The optimum concentration for a given situation has always fallen within the range 20-60 percent. Dioxane in water in concentrations of less than 50 percent has been found best in some cases, but some doubt remains as to the effect of the dioxane on the sections. Some corrosion-retarding agent should be used in the liquid, particularly in the case of dioxane in water. The addition of one part per thousand of chromoglucosate has been very satisfactory for this purpose. The criteria for the adjustment of the concentration of the liquid have been developed from continuous observation of the cutting through a stereoscopic microscope ( $\times 27$ ) and from correlation with the quality of the sections, as judged in the light and electron microscopes ( $\times 400$  and  $\times 1000-5000$ ), respectively.

Another important parameter in the adjustment of the liquid is its level relative to the edge. It has been found empirically that the best sections are obtained when the level is maintained as high as possible. The limiting condition in this regard is that the block must remain dry for a sufficiently long series of sections. It is further determined by a number of factors relating to the nature of the tissue, its fixation, its embedding, the sharpness and cleanliness of the knife, the clearance angle, and the nature of the liquid. The correct level is found by raising the height of the liquid slowly as sections are being cut and observed at a magnification of at least nine times. When the level is slightly too high, a small area will be wet by the liquid. Moreover, the wet area will increase with

each successive cut. It is a simple matter to achieve this condition and then to lower the level until the wet area diminishes and disappears. If, by accident, the entire face of the block gets wet, the situation can be corrected by lowering the level of the liquid approximately 1 mm below the edge of the blade until the sections appear dry. The correction can be hurried by drying the back of the knife and the face of the block with absorbent cotton.

This system of collecting specimens as they are cut has fulfilled very satisfactorily its intended purpose of providing serial sections. It has also made two unexpected but welcome contributions to the program, in that it provided sensitive criteria for detecting irregularities in the performance of the advancing mechanism of the microtome and for judging the quality of the sections even before they are examined in the electron microscope. It is the practice in this laboratory to examine sections at magnifications of nine times or twenty-seven times as they are cut. It was soon realized that for a given knife, block, liquid, etc., the length of a floating section (measured in the direction of cutting) or, conversely, the apparent compression is a sensitive criterion for the thickness of the layer removed from the block—that is, the magnitude of the advance. Since, by this means, any irregularities in the magnitude of successive advances (as small as 5 percent) are immediately observable, it is a relatively simple matter to identify and eliminate the various sources (2).

Continuous observation of the sections as they are cut and correlation with the results obtained in the electron microscope showed that satisfactory sections appear on the surface of the liquid instantaneously and completely extended, as each cut is made. Moreover, they appear quite transparent and almost invisible. On the other hand, an unsatisfactory section seems to slide slowly to the surface from a folded condition near the edge of the knife, and it never attains the transparency of the satisfactory sections. It has also been found that the height to which the liquid can be raised without wetting the block is a good criterion of section quality. No good sections have been obtained when difficulty has been encountered in achieving a plane or convex meniscus, though it is not to be implied that such a meniscus is necessary to successful cutting.

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# Technical Papers

## The *in Vitro* Production of Cortisone by Mammalian Cells

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Recently favorable clinical results were obtained through the combined use of desoxycorticosterone acetate and ascorbic acid in the treatment of rheumatoid arthritis in Europe and America (1, 2, 3, 4). It was reasoned

were devised where the cortical tissue obtained from healthy animals was incubated in suitably enriched media with desoxycorticosterone. The steroids<sup>2</sup> were extracted from the medium and tested chemically by the paper chromatography method of Zaffaroni, Burton, and Keutman (5).

The culture medium used in these experiments contained equal amounts of Penassay broth (Difco) and Seneca hemoflagellate broth (6), adjusted to pH 7.5 with  $\text{Na}_2\text{HPO}_4$ . Fifty to 100 ml of this broth was put in 250-ml Erlenmeyer flasks and autoclaved. After cooling, human plasma was added to make 10% of the medium. To the first flask the following vitamins were added under sterile conditions: 1 ml of 10% ascorbic acid (100 mg), 2.5 ml of 1% thiamine hydrochloride (25 mg), and

TABLE 1  
PRODUCTION OF CORTISONE FROM DESOXYCORTICOSTERONE BY VARIOUS TISSUES INCUBATED  
IN ENRICHED SENECA-PENASSAY BROTH

Flask No.	8	2	1	7	3	5	6	4
Tissue	DOC	DOC Vit. C	DOC Vit. C Vit. $\text{B}_1\text{B}_2\text{B}_6$ Nic. Ac.	DOC Vit. C Vit. $\text{B}_1\text{B}_2\text{B}_6$ Nic. Ac. insulin.	DOC Insulin	DOC Gluta- thione	DOC Gluta- thione Vit. C Vit. $\text{B}_1\text{B}_2\text{B}_6$ Nic. Ac.	DOC Gluta- thione Vit. C Vit. $\text{B}_1\text{B}_2\text{B}_6$ Nic. Ac. insulin
Adrenal	+ or -	+	++	+++	+++	-	-	-
Liver				+ or ++				
Testis				+ or ++				
Kidney				+				
Ovary				- or +				
Cardiac muscle				-				
Striped muscle				-				
Spleen				-				
Lung				-				
Brain				-				
Thyroid				-				
Bone marrow				-				
Pancreas				-				
Placenta				-				
Prostate				-				

+++ = positive in over 75% of tissue or gland tested.  
++ = " in over 50% of " " " "  
+ = " in 25 to 50% of " " " "  
+ = " in about 25% of " " " "  
+ or - = occasionally positive.  
- = no production of glucocorticoid.

that oxidizing and reducing agents, especially in conjunction with the oxidation-reduction enzyme systems of the adrenal cortical cells, probably could synthesize cortisone from desoxycorticosterone or its precursors. Experiments

0.5 ml 1% riboflavin, 1% pyridoxine, and 1% nicotinic acid (5 mg each). To the second flask 1 ml of 10% ascorbic acid (100 mg) was added; to the third flask, 5 units of insulin; to the fourth, all vitamins, plus 5 units insulin; to the fifth, 0.5 ml of 1% glutathione (5 mg); to the sixth, 5 mg glutathione and vitamins; to the seventh, 5 units insulin, 5 mg glutathione, and all vitamins. The eighth flask was control, containing only broth. To

<sup>2</sup> The steroids were obtained through the courtesy of Schering Corporation, Bloomfield, N. J.

<sup>1</sup> U. S. Public Health Service Postdoctorate Research Fellow.



all the flasks, 15 mg of desoxycorticosterone was added. Desoxycorticosterone in 150-mg quantity was dissolved in 33.4 ml propylene glycol and 16.6 ml distilled water. Autoclaving readily dissolved the steroid and sterilized it. Five ml was added to each flask.

The adrenal glands of cats, dogs, rats, guinea pigs, and chickens were removed under sterile technique while the animals were under ether anesthesia. Half a human adrenal from a case of Cushing syndrome removed by operation was also tested. Immediately following the removal, with the least lapse of time and manipulation, the glands were sliced with a sharp razor blade into 3 or 4 longitudinal slices, and placed in the flasks containing the medium and ingredients. To prevent bacterial contamination, 10,000 or 50,000 units of penicillin G were added. The flasks were incubated at 37° C, and every 48 hr the medium was replaced by freshly made broth and ingredients, on three occasions.

In another series of experiments, slices of the kidney, liver, ovary, testis, cardiac muscle, striped muscle, spleen, lung, brain, thyroid, bone marrow, and pancreas of the cat, dog, and rat, as well as human placenta and human prostate, were incubated in broth containing 15 mg desoxycorticosterone, 100 mg ascorbic acid, 25 mg thiamine, 5 mg pyridoxine, 5 mg riboflavin, 5 mg nicotinic acid, and 5 units of insulin. The broth in the flasks with the glandular tissue was kept sterile by the addition of penicillin G. The medium was changed every 48 hr on three occasions by substituting freshly made medium.

Fresh adrenals, kidneys, testis, and human placenta were separately tested for the presence of cortisone. The glandular tissue was ground up with glass sand in a mortar and extracted with either 20% trichloroacetic acid or *N* HCl, or both, for 25 hr at 37° C. It was then extracted with ether, *N*/10, NaOH and then *N* HCl. This neutral extract was then tested for the presence of cortisone by paper chromatography.

Each sample of broth obtained from the culture flasks every 48 hr was tested for the presence of cortisone. Samples of the adrenal gland were removed at 24-hr intervals throughout the period of incubation and preserved in 10% formalin for histological studies. The broth was first adjusted to pH 1 with *N* HCl. The proteins were then precipitated with 20% trichloroacetic acid. The supernatant and the precipitate were then extracted separately with ether, and then the extracts were combined, washed with *N*/10 NaOH and then *N* HCl, and finally evaporated to about 5 ml. The extracts were then tested individually for the presence of cortisone by the propylene-toluene chromatography method at the end of 72 hr, by spraying with 5% potassium iodide and 0.3% iodine solution.

The following results were obtained in these experiments:

1. Extracts of adrenals, liver, kidneys, testis, and human placenta were negative for cortisone. Table 1 shows the result of incubating various tissues with desoxycorticosterone, vitamins, and insulin.

2. Incubation of adrenal in media containing desoxycorticosterone, insulin, ascorbic acid, thiamine, pyridoxine,

riboflavin, and nicotinic acid gave the most constant and potent paper chromatography test. Most of the positives were obtained in the second sample of broth. It was almost always negative in the first 48 hr of incubation. Positive results were also obtained in the third sample of broth.

3. Desoxycorticosterone plus adrenal gland and insulin gave the second highest positive; vitamin B complex was next, followed by ascorbic acid, although sometimes simple incubation of adrenals with desoxycorticosterone also yielded positive results.

4. When desoxycorticosterone and adrenal gland were incubated with glutathione, or with glutathione, insulin, ascorbic acid, and vitamin B complex, the results were consistently negative.

5. Positive chromatograms were obtained in a third of the experiments where the liver or testis was incubated with desoxycorticosterone, insulin, ascorbic acid and thiamine, riboflavin, pyridoxine, and nicotinic acid. The kidney and, to a lesser extent, the ovary also gave positive chromatograms.

6. All the other tissues tested gave negative results.

7. The adrenals of the cat and man (one case tested) gave the highest positives, followed by those of the dog, rat, and guinea pig, in the order cited, whereas the adrenal of the chicken was always negative.

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### On the Detection of Intracranial Pathology by Ultrasound<sup>1</sup>

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This report deals with the initial progress of a long-range program on the application of ultrasonic techniques to medical problems (1). An immediate goal is the detection and localization of intracranial tumors and cerebral anatomic abnormalities.

There are two basic methods of using ultrasound for diagnosis. One uses echoes reflected from interfaces within an object, the other utilizes selective transmission through an object. In either method the useful range of vibration frequency appears to be of the order of a

<sup>1</sup>A report from the Medical Acoustics Research Project, being undertaken collaboratively by MIT and the Massachusetts General Hospital, and supported by funds from an Institutional Grant to the Massachusetts General Hospital from the American Cancer Society and a grant from the Submarine Signal Division of the Raytheon Manufacturing Company to MIT. Presented, in part, at a meeting of the American Neurological Association, Atlantic City, N. J., June 12, 1950.

few megacycles per second, and ultrasound in this range is conveniently generated and detected by piezoelectric crystals. A comparative study of these two approaches has led us to investigate first the transmission method.

The rationale for attempting to employ such a technique for the detection of intracranial lesions is based on the following facts: When a beam of ultrasound is sent through a portion of tissue, the amount of energy that arrives at a receiver is influenced by absorption along the path, by refraction and scattering, and by reflections at any intervening interfaces. These acoustic variables in turn are determined by such physical properties of tissue as density, elasticity, homogeneity, and viscosity.

The influence of these different properties of living matter on high-frequency sound waves is not generally the same as on other forms of physical energy, such as the electromagnetic radiation of x-rays. The attenuation of ultrasound as it traverses the fluid-filled ventricles is less than that through cerebral tissue. Utilizing this property, Dussik *et al.* (2) have obtained ultrasonic ventriculograms on a large number of patients. The purpose of our work is to refine and extend this method, and to study the basic physical and physiological problems involved.

At present x-ray evidence of distortion of the ventricular system is of great value in the diagnosis of neurological disorders. To obtain this information, however, the ventricular fluid must be replaced by air. A method that would yield substantially the same information, but without the necessity for air injection, would constitute a distinct improvement over present techniques.

It has also been shown that ultrasound may produce tissue damage. The skin, for example, will be injured by a minimum intensity of 5 w/cm<sup>2</sup> peak, if continuous irradiation is applied to a given area for 10 min at a frequency of 800 kc (3). Pain, which seems to come from deep within the tissues and is presumed to originate at the pericosteum, will occur when an intensity of 2 w/cm<sup>2</sup> peak is applied for 40 sec at this same frequency (4). Below 1.8 w/cm<sup>2</sup> no pain is caused, irrespective of the duration of irradiation. The Dussiks were able to record a received signal from a beam of transcranially transmitted ultrasound the intensity of which at the transmitter was about 1 w/cm<sup>2</sup>. They report no evidence of brain damage from the use of this intensity on more than 200 patients. On a theoretical basis this seems likely, because ultrasound at a frequency of 800 kc is attenuated about 30 db as it travels through scalp, subcutaneous tissue, and skull; the intensity that reaches the first cortical layer of the brain is so low that, according to all available evidence, it would be incapable of damaging living tissue, regardless of the duration of application.

Nevertheless, we have been unable to find experimental evidence as to the maximum intensity and duration of application that can be applied to a given area of nervous tissue without producing interruption of function (5). We are in the process of investigating this problem and to date have irradiated transdermally 2 dogs, a cat, and

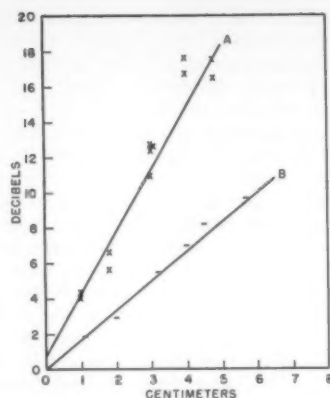


FIG. 1. Attenuation measurements in fresh hog-brain: A through whole brain including cortical convolutions; B, through blocks of white matter.

2 human subjects. The 2 dogs were exposed to ultrasound at a frequency of 2.4 Mc. In one, an intensity of 3 w/cm<sup>2</sup> was applied for 11.5 min; in the other, an intensity of 1.5 w/cm<sup>2</sup> was applied for 15 min. In neither animal was histological evidence of brain damage found.

The cat was exposed to a frequency of 800 kc at an intensity of 15 w/cm<sup>2</sup> for 5 min. Electroencephalographic recordings taken during the period of radiation showed no pathological changes. The animal suffered superficial scalp necrosis but showed no evidence of neurological deficit.

The 2 human subjects were also irradiated by placing the 800-kc transmitter in contact with the scalp and using electroencephalographic control. Peak intensities of the order of 5 w/cm<sup>2</sup> (2 w/cm<sup>2</sup> average over the irradiated surface) for periods up to 9 sec were sufficient to cause moderate scalp pain but did not alter the pattern of the EEG.

Since the success of the transmission method depends basically on whether there is sufficient difference in the attenuation of ultrasound as it passes through cerebral tissue with and without ventricle, measurements of attenuation in tissue, including brain, have been made with frequencies of 1.25 Mc and 2.5 Mc (6). Fig. 1 shows the attenuation of fresh hog brain as a function of sample thickness. Curve A represents measurements on whole brain, curve B measurements on blocks of brain tissue containing white matter only. Average attenuation in A is 4 db/cm, and in B it is 1.7 db/cm. Measurements on human brain are in agreement with these findings. Ultrasound at these frequencies is attenuated about 50 db/cm by the bones of the skull.

The interposition of the ventricular system in the path of an ultrasonic "beam" that is scanning the brain increases the energy received by amounts up to 20 db (a factor of 10 in voltage). This differential is more than sufficient to indicate the position of the ventricles.

In the apparatus used for these measurements, a pencil-

shaped ultrasonic beam is generated by a barium titanate transducer, which is driven by a stable c-w transmitter, modulated with 1,000 cps. This transducer has a rectangular aperture of 1 cm<sup>2</sup> and is mounted in a water tank opposite a receiver crystal (quartz) of variable aperture. The test object is supported between the 2 probes. The received signal is amplified, demodulated, and fed into a sound level recorder.

In one of our experiments a formalin-fixed brain was scanned by the ultrasonic beam. The line of scan was marked by small lead pellets, the ventricular system injected with diodrast, and a lateral radiograph obtained. Fig. 2 shows the degree of correlation achieved between

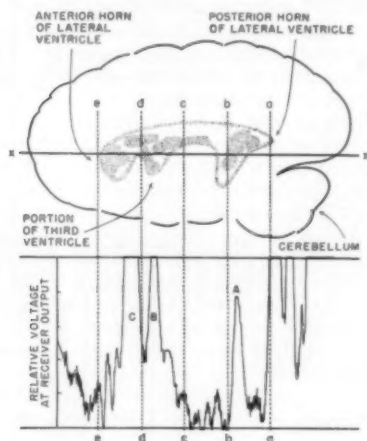


FIG. 2. Correlation between x-ray ventriculogram and ultrasonogram.

the two methods. The upper half of the illustration is a drawing of the brain specimen, with shading of those areas of the ventricular system most capable of being filled by diodrast. The line *x-x* is the line of scan, and the lower half of the figure is a reproduction of the sound level recording. At first the received signal is high in consequence of the decreased path through the tips of the frontal lobes. As they begin to increase in size, signal strength diminishes until the anterior horns of the ventricles are reached at *c*. The two peaks *C* and *B* on the ultrasonogram correspond to the shaded areas to the left and right of point *d*. The strong signal at *C* indicates the position of the largest portion of the anterior horns of the ventricles. Decreased signal strength appears at *c* and *b* as the sound beam passes out of the ventricles. At *A* another strong signal appears as the posterior portion of the lateral ventricles is partially traversed. To the right of *a* the signal strength again increases because of the decreasing path through the occipital lobes. In transcranial scanning this is compensated for by a greater energy loss resulting from oblique incidence of the rays as they strike the frontal and occipital regions of the skull.

Fig. 3 is a record taken on a living human subject in

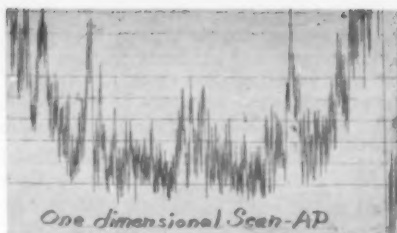


FIG. 3. Recording of live subject made in the unmodified tank, showing masking effect of reverberation.

an anterior-posterior direction. Symmetrical peaks that are believed to be significant appear on either half of the record. There is, however, a considerable amount of background "noise" from reverberant sound, and the attenuation caused by the skull is sufficient in some cases to bring the received signal down to levels below the reverberant intensity. Therefore, the tank had to be subdivided into 2 compartments sonically insulated from each other by the head. The new arrangement shown in Fig. 4 prevents leakage of reverberation from the transmitter compartment to the receiver compartment, both of which are lined with absorbent material to damp the undesired waves.

A simple recording device has been added to this apparatus in order to produce a contrast recording of a two-dimensional scan of the brain. We have been able to portray crudely the position of the ventricular systems of 3 normal subjects using this apparatus. No pain or other untoward effect has been produced. The intensity employed was less than 1 w/cm<sup>2</sup> at a frequency of 2.5 Mc.

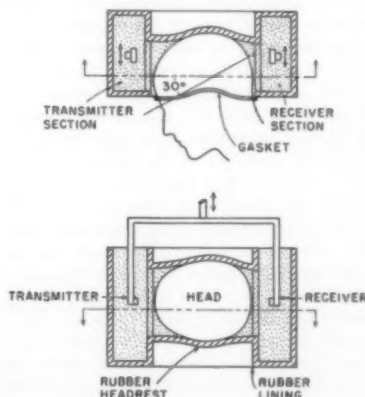


FIG. 4. Schematic diagram of tank for scanning brain of live subjects.

These investigations have demonstrated that an ultrasonic transmission method can yield ventriculograms without air injection by utilizing a level of intensity below any known threshold of pain or damage. The possibility also exists that types of brain tumors which exhibit

a sufficient degree of either calcification or cyst formation may be detected directly if there is sufficient difference in attenuation of ultrasound by these tumors in comparison to normal cerebral tissue. To establish the ultimate capabilities and limitations of ultrasonic methods, we are pursuing a number of fundamental studies on the behavior of ultrasound in biological tissues.

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### A Slicer for Sampling Liquids<sup>1</sup>

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A mechanical slicer has been developed for sampling various levels of liquids contained in plastic tubes. This technique obtains small, accurately determined samples, with a minimum of stirring, and with high volumetric recovery.

Fig. 1 presents two views of such a slicer designed for  $\frac{1}{2}$ -in. diameter plastic tubes of 8.2-cc capacity used in a quantity ultracentrifuge. The plastic tube *T*, filled with liquid to be sampled, is held by clamps *C* in plastic plates *P* and *Q* just above and below the desired level of division. A very thin (.007-in.) knife blade *B* made from razor blade stock<sup>3</sup> is carried in a rigid frame *F*, which slides in ways *W* machined in the plates. This frame is moved by a lever *L*. The sharpened edge of the blade cuts the tube wall, and the flat body of the blade serves as a sealing partition between the upper and lower levels of liquid. The plates are held together by two compressed springs *CS* adjusted to prevent leakage of the liquid above the blade. The upper liquid sample is removed with a hypodermic syringe or pipette. The clamps are loosened, the top section of the plastic tube is removed, and the blade withdrawn. A screw drive *D*, carrying an indicator *I*, which reads against a fixed scale *S*, raises the remaining portion of the tube to the level

of the next slice, and the entire operation is repeated.

In order to prevent loss of liquid because of capillary action if surfaces become wet, a nonwetting grease is spread over the knife blade and other parts near the tube. We have used a mixture of 3 parts vaseline to 1 part mineral oil for this purpose, although probably a silicone grease is preferable. Since such greases are almost insoluble and chemically inert, this procedure will seldom affect subsequent analyses of the samples. Grease cups

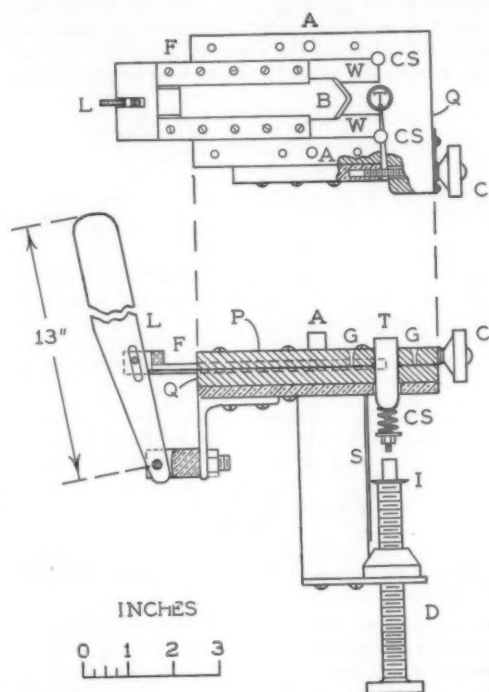


FIG. 1.

*G*, tapered to fit a hypodermic syringe, permit adding grease at any time.

For stability, the device is held in a heavy vise or bolted to a workbench. None of the dimensions is critical save that the plates must bear against the blade to insure proper slicing. In our instruments, each of the springs exerts a force of about 15 pounds. Our plates are made from  $\frac{1}{8}$ -in. Plexiglas, with tapered pins *A* to insure alignment.

Using this technique to sample groups of three 8.2-cc tubes of ultracentrifuged serum, we recover about 92% of the liquid when dividing each tube into 10 samples. Part of the volume lost remains on the walls of the plastic tube and part in the 10 hypodermic syringes used. These residues are increased by the high viscosities in the lower regions of each tube, where we find 30g% of protein. Sampling similar tubes filled with water and using only one syringe, we recover 99% or more of the volume.

<sup>1</sup>This work has been supported in part by a grant from the Committee on Growth, acting for the American Cancer Society.

<sup>2</sup>We wish to express our appreciation to R. H. Turner and his group for the suggestion of this device and for encouragement during its development.

<sup>3</sup>We are grateful to Howard Gambrill, Jr., of the Gillette Razor Blade Company, Boston, Mass., for this stock.

# Effects of Different Preincubation Temperatures on the Hatchability of Pheasant Eggs

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Although there has been much speculation as to the cause of widespread failure of pheasants, *Phasianus*,<sup>1</sup> to become established in the southern United States, no field studies of the limiting factors in or near the unoccupied zone have been reported. Climatographic studies have given evidence that the breeding ranges of several introduced birds may be limited by meteorological influences. Twomey (6) showed similarities of temperature and rainfall in the European and North American ranges during breeding seasons of the European skylark, *Alauda arvensis*, and the Hungarian partridge, *Perdix p. perdix*. Bennett and Terrill (5) reported that the southern limit of pheasant range east of the Great Plains follows closely Thorntwaite's line separating microthermal from mesothermal climates. Graham and Hesterberg (4) showed that means of temperature and rainfall in different parts of the optimum pheasant range in the United States are very similar during April and May, when the peak of nest establishment occurs, even though they may be at wide variance during the remainder of the year. These authors postulated that in southern latitudes very young pheasant embryos are killed by intense insolation of the exposed eggs while the clutches are being laid.

In the north-central region, highest pheasant populations occur in the northern tier of states and in the northern parts of Iowa, Illinois, Indiana, and Ohio. Hatching there usually reaches a peak during the first 3 weeks of June (often followed by another peak when a large portion of the early nesting attempts are unsuccessful) and continues at a declining rate until late summer (1). Brood studies since 1937 in central Illinois, near the southern limit of range, frequently have shown a sharp decrease of successful hatches and in number of young per brood about the first week in July. Nest studies indicated that this decrease is chiefly the result of a decline in hatchability of the eggs. For example, in 1947 and 1948, 68 (42.6%) of the 147 fertile eggs in 16 nests where some young hatched after July 1 contained dead embryos, usually at a very early stage of development. A number of subnormal young which died in the nests or soon after leaving them have been found in late hatches also. This study will be reported more fully elsewhere.

In hatchability studies at Urbana in 1948 and 1949, eggs of the bobwhite *Colinus virginianus* were compared with pheasant eggs by simultaneous exposure to the same range of experimental conditions. This comparison was

believed useful because the bobwhite breeds in suitable habitat both inside and outside the Illinois pheasant range, and its breeding cycle grossly resembles that of the pheasant.

Fresh-laid pheasant and bobwhite eggs were obtained from the breeding pens of the Illinois Department of Conservation for these studies. Samples of 60 pheasant eggs laid in mid-June, 1948, failed to hatch after 14 days' exposure in shade to air temperatures varying from 51° F to 88° F, mean 72.3° F, and recorded relative humidities of 34%-100%, without prolonged rainfall or drought. Bobwhite eggs so exposed showed no apparent decline of hatchability after 19 days, nor did bobwhite eggs exposed to an additional 30 min of solar radiation in mid-day for 5 days. Low retention of hatchability by pheasant eggs and high retention by bobwhite eggs were also found in each of several outdoor exposures of 10 days or more in late June and early July, 1949.

Pheasant and bobwhite eggs laid on May 31, 1949, were used in a controlled experiment to test the effect on hatchability of air temperatures normally experienced in late spring in central Illinois. Fertility shown by Kocin's method (5) was above 95% for both species. It was assumed from observed growth and survival of wild and game farm birds that vigor of the embryos of both pheasants and bobwhites at this time would be high. Paired lots of pheasant and bobwhite eggs were placed in 4 small electric incubators without forced draft (7) and exposed continuously from 8 A.M. to 5 P.M. for 7 days prior to incubation, to 4 different temperatures from 73° F to 88° F. Because the average time of clutch-laying is approximately 12 days for pheasants and 18 days for bobwhites, the 7-day exposure was used to test the effect of temperature on eggs laid midway in the production of clutches. The eggs thus exposed were kept in a temperature control chamber at 62° F during the remaining 15 hr of each day. Controls were kept continuously at 62° F. Relative humidity of 65% was constant. All eggs were turned twice daily.

Incubation of these exposed and control eggs indicated (Table 1) that the hatchability of pheasant eggs was

TABLE 1  
HATCHABILITY OF PHEASANT AND BOBWHITE EGGS EXPOSED TO DIFFERENT PREINCUBATION TEMPERATURES

Temperature	No. fertile pheasant eggs	Hatchability, %	No. fertile bobwhite eggs	Hatchability, %
Controls (62° F)	40	75.0	42	76.2
73° F	39	64.1	39	79.5
78° F	42	64.3	39	69.2
83° F	37	45.9	40	75.0
88° F	38	42.1	38	68.4

reduced by heat exposures, the reduction increasing with the higher temperatures. As was found previously in eggs from late wild nests, about 70% of the dead pheasant embryos in the heat-exposed eggs died prior to

<sup>1</sup> Hybrids believed mainly of *P. t. torquatus*, native to eastern China and northern Indo-China, and *P. c. colchicus* of western Transcaucasia are widely distributed in the United States north of latitude 40°. In the Pacific Northwest, *P. t. torquatus* is found quite pure in certain regions (3).



the 48-hr stage. No significant reduction of hatchability of the bobwhite eggs by high temperatures was evident.

It seems probable that vulnerability of pheasant embryos to air temperature during the laying period has an important influence in limiting the southern distribution of pheasants. Pheasants reported breeding locally in the southern Pacific Coast and Rocky Mountain regions may be predominantly of southern Asiatic origin, and possibly thus more tolerant of higher temperatures.

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## Distribution of Absorbed Energy around a Point Source of $\beta$ Radiation<sup>1</sup>

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The radiation dose delivered to tissue by sources of  $\beta$  radiation distributed through the tissue is easily computed in the interior of a uniform distribution in homogeneous tissue (1). The energy delivered to the tissue per second is just the energy emitted by the  $\beta$  radiation per second. Moreover, on the edge of such a homogeneous distribution, at a surface facing tissue free of  $\beta$  emitter, the dose is just half that at the interior. These two simple statements exhaust the generally available information on the distribution of tissue dose caused by  $\beta$  emitters. In order to compute the absorbed energy (or observed ionization) about an arbitrary distribution, it is necessary to know the spherically symmetrical function which gives these quantities as a function of distance from a point source of  $\beta$  radiation in absorbing material.

The direct measurement of the radial ionization function around a point source presents a difficult experimental problem. If attempted in unit density material, the spherical isoionization surfaces will not conform to a practical ionization chamber. If attempted in air, the scattering off the source, external objects, and the ionization chamber will be sources of error, as well as absorption in the walls of the ionization chamber. By using a plane source and plane ionization chamber in unit density material, these difficulties can be avoided. The method is based on the fact that the ionization per cc ( $I_r$ ) in a vanishingly small cavity in an absorbing material trav-

ersed by a flux of ionizing radiation is related to the energy absorbed per cc ( $E_r$ ) by the equation

$$I_r = E_r / \rho W,$$

where  $\rho$  is the stopping power of the absorbing material relative to the gas in the cavity, and  $W$  is the average energy per ion pair formed in the gas of the cavity for the ionizing particles (2).

Consider now a point source of  $\beta$  radiation in an "infinite" (i.e., larger than the maximum  $\beta$  range) block of unit density absorbing material of low atomic number. Let the energy absorbed in a very thin spherical shell around the point source be

$$4\pi r^2 I(r) dr \text{ energy/disintegration.}$$

Then the total energy absorbed per disintegration is the average  $\beta$  particle energy

$$\bar{E}_\beta = 4\pi \int_0^\infty r^2 I(r) dr.$$

By straightforward integration of  $I(r)$ , and using the first equation given, it follows that the ionization that will occur in a very thin, plane air gap parallel to a very thin, plane source in a large block of material is given by

$$D(z) = \frac{2\pi\sigma}{\rho W} \int_z^\infty r I(r) dr \text{ ion pairs/cc,}$$

where  $\sigma$  is the surface intensity of the source in disintegrations/cm<sup>2</sup>, and  $z$  is the perpendicular distance from the source to the air gap. It is easy to show that

$$\sigma = 2\kappa\rho W / \bar{E}_\beta, \quad \text{where } \kappa = \int_0^\infty D(z) dz.$$

It follows that the point source function can be obtained from the equation

$$I(r) = \frac{\bar{E}_\beta}{4\pi\kappa} \frac{1}{r} \left( -\frac{dD}{dr} \right) \text{ (energy/disintegration)/cc.}$$

Thus we have an explicit method of computing the radial energy absorption about a point source of  $\beta$  radiation, if measurements are made of the ionization normal to a very thin source. It is seen that  $D(z)$  may be arbitrarily multiplied by any constant without affecting the value of  $I(r)$ . As a result, only relative ionization measurements need be made. Moreover, the numerical value of  $\rho$  and  $W$  do not enter into the calculation of  $I(r)$ , to the extent that they are independent of the energy of the  $\beta$  particles.

The experiment has been performed with radioactive phosphorus. Sources not thicker than 0.05 mg/cm<sup>2</sup> were prepared by spraying a solution of P<sup>32</sup> onto a plane block of polystyrene with a penicillin nebulizer. The absorbing material was sprayed carbon of about 0.1 mg/cm<sup>2</sup>, nylon of about 1 mg/cm<sup>2</sup>, and polystyrene from 2 to 10<sup>4</sup> mg/cm<sup>2</sup>. Measurements were made in a parallel-plate ionization chamber of variable air gap, using a vibrating reed electrometer.<sup>2</sup> The electrodes were carbon-sprayed onto

<sup>1</sup>This work was done in part under contract with the Atomic Energy Commission, and in part with the support of the Committee on Growth of the American Cancer Society.

<sup>2</sup>The basic design of the ionization chamber used is that of G. Failla and N. Baily, of the College of Physicians and Surgeons, New York City. The instrument was designed and constructed by the Instruments Branch, Medical Division, New York Office, AEC (H. D. LeVine, chief, and H. J. DiGiovanni, assistant chief).

polystyrene or nylon, to a thickness of not greater than 0.1 mg/cm<sup>2</sup>. The collecting diameter was defined by a circle scribed in the carbon and was surrounded by a guard ring. The air gap was determined by a capacity measurement for each measurement of ionization current. The ionization per unit volume was determined for several different air gaps, and extrapolated to zero air gap, for each absorber thickness. The measuring volume was at all times surrounded by an "infinite" thickness of polystyrene.

The observed ionization due to the thin sources had the functional form

$$\begin{aligned} D(s) &= A - B \ln s & 0 < s < 200 \text{ mg/cm}^2 \\ D(s) &= C \exp(-\mu s) & 80 < s. \end{aligned}$$

The constants  $A$ ,  $B$ , and the joining point  $s_1$  can be determined in terms of  $\mu$  by using the conditions that  $D(s)$ , the point source function  $I(r)$ , and the first derivative of  $I(r)$  must be continuous at the joining point. The remaining constant,  $C$ , can be fixed at any convenient value, because of the arbitrary multiplicative constant in  $D(s)$ . Then the ionization, in arbitrary units, normal to a thin plane source is given by

$$\begin{aligned} D(s) &= 1 - \ln \mu s & 0 < \mu s \leq 1 \\ D(s) &= \exp(1 - \mu s) & 1 \leq \mu s, \end{aligned}$$

where  $\mu s_1 = 1$ . It is found experimentally that  $\mu = 9.10$  cm<sup>2</sup>/g, and hence  $s_1 = 110$  mg/cm<sup>2</sup> for P<sup>32</sup>. Since the last equations imply  $\kappa = 3/\mu$ , we get for the distribution of absorbed energy around a point source of P<sup>32</sup> in polystyrene

$$\begin{aligned} I(r) &= \frac{\bar{E}_\beta \mu^2}{12\pi} f(\mu r) & (\text{energy/dia})/\text{cc}, \\ \text{where } f(\mu r) &= 1/(\mu r)^2, & 0 < \mu r \leq 1 \\ f(\mu r) &= (1/\mu r) \exp(1 - \mu r), & 1 \leq \mu r. \end{aligned}$$

It is implied that the point source is contained in a block of the absorbing material larger in all directions than the maximum range of the  $\beta$  particles. Then the dose at a distance  $r$  from a small volume  $dV$  cc containing  $C$   $\mu\text{c/g}$  of  $\beta$  emitter is given by

$$0.0608 \bar{E}_\beta C f(\mu r) \mu^2 dV \text{ rep/hr},$$

where now  $\bar{E}_\beta$  is the average  $\beta$  energy per disintegration in mev and has the value 0.695 for P<sup>32</sup> (3). The rep (roentgen equivalent physical) has been taken as 93 ergs/g of absorbed energy (4), so the resultant dose rate will be 12% lower than in earlier publications, which used the figure 83 ergs/g (1). In using this formula for computation, the products  $\mu r$  and  $\mu^2 dV$  are dimensionless. With this result, it is a straightforward matter to compute the dose due to any known distribution of  $\beta$  emitter, though only the relatively simple sources such as plane slabs and spheres can be computed in analytic form.

The noteworthy features of the result are these: (1) the dose is given by simple, analytical functions; (2) only two physical parameters are involved in the calculations,  $\bar{E}_\beta$  and  $\mu$ , the first affecting the magnitude and the second the distribution of the dose; (3) the entire dose distribution calculation can be carried out in dimensionless equations if the unit of distance is taken as  $s_1 = 1/\mu$ ; and (4) the initial attenuation around a point source is inverse square.

The experimental value of  $D(s)$  is actually not exponential out to the end of the  $\beta$  range, as the equations would imply, but begins to be measurably less than the exponential values for  $s \approx 400$  mg/cm<sup>2</sup>. The intensity at these distances is, however, so small that, at least for biological and medical dose calculations, the equations as stated are entirely adequate.

A few measurements are available on thick sources of other isotopes (5). From these it is provisionally concluded that the same type of analysis can be made for other  $\beta$  emitters, and that the product  $\mu \bar{E}_\beta$  is approximately constant for all  $\beta$  emitters. Under these circumstances, a calculation of dose distribution for  $\beta$  sources in tissue can be made in dimensionless form, and then applied to any  $\beta$ -emitting isotope for which the mean  $\beta$  energy is known or can be computed. Measurements on other isotopes are now under way. Full details will be published elsewhere.

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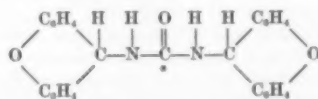
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## Errors of Combustion of Compounds for C<sup>14</sup> Analysis<sup>1</sup>

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The precipitation of xanthidrol ureide affords a simple method for the isolation of urea from urine and has been used for this purpose in tracer studies with radio-carbon (5, 13). Xanthidrol ureide labeled with radio-carbon only in the urea residue, as indicated in the formula below by an asterisk, was prepared in a previous study (3) from the urine of a rat.



Large discrepancies were noted between C<sup>14</sup> assay of some of the preparations of barium carbonate obtained by wet oxidation of the compound with the Van Slyke-Folch (12) solution, when the technique described by Lindenbaum, Schubert, and Armstrong was used (6). The investiga-

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TABLE 1  
RADIOCARBON ASSAYS OF BARIUM CARBONATE OBTAINED BY  
FRACTIONAL COLLECTION OF CARBON DIOXIDE DERIVED  
FROM COMBUSTION OF XANTHYDROL UREIDE

Method of combustion	Fraction No.	% carbon found*	C <sup>14</sup> specific activity cpm/mg C
Wet	1	6.7	2.4 ± 0.2
	2	18.1	2.2 ± 0.2
	3	25.4	0.6 ± 0.1
	4	14.8	2.1 ± 0.2
	5	12.4	3.2 ± 0.2
	6	22.6	1065.9 ± 4.6
Dry	1	40.8	458.3 ± 3.1
	2	59.2	106.1 ± 1.1

\* Percentage of recovered carbon in each fraction.

tion of these discrepancies in radioactivity assay revealed large differences between the rates of conversion to carbon dioxide of carbon atoms occupying the labeled, and those occupying the unlabeled, positions in xanthidrol ureide. These differences, as shown in Table 1, were noted when both wet and dry oxidation methods were used. Because of these findings the work was extended to demonstrate discrimination between carbon isotopes when C<sup>14</sup>-labeled urea was converted to CO<sub>2</sub> by wet oxidation. Our observations are reported because of their bearing on the methods used for combustion of labeled compounds preparatory to carbon isotope assay, and because they contribute to the general subject of the influence of isotopes on chemical behavior.

No instance has heretofore been noted of differences in the order of conversion of the carbon atoms of a compound to CO<sub>2</sub> on complete oxidation of the compound. However, discrimination between carbon isotopes in chemical reactions other than oxidation has been described. An 8% greater frequency of rupture of the C<sup>12</sup>-C<sup>13</sup> bond than of the C<sup>12</sup>-C<sup>14</sup> bond was found on partial thermal cracking of propane-1-C<sup>13</sup> (11). Yankwich and Calvin (14) found that thermal decarboxylation of malonic acid singly labeled in a carboxyl group with C<sup>14</sup> resulted in acetic acid with a C<sup>14</sup> content 12% greater than that of the CO<sub>2</sub> evolved. With the use of the C<sup>13</sup> naturally occurring in oxalic acid as an indicator, the decomposition of this substance in hot sulphuric acid to CO<sub>2</sub>, CO, and H<sub>2</sub>O was investigated (7). A preference was found for C<sup>13</sup> in the CO<sub>2</sub> rather than in the CO. A preference was noted also for a higher rate of decomposition of oxalic acid molecules containing only C<sup>13</sup> than of those containing both C<sup>13</sup> and C<sup>14</sup>. In a study (8) of the hydrolysis of C<sup>14</sup>-labeled urea by urease enzyme, it was observed that the first fractions of CO<sub>2</sub> evolved were relatively richer in C<sup>14</sup> than those produced in later stages of the reaction. The authors indicated that the opposite result is to be expected if the only factor affecting reaction rates is the zero point energy of the C<sup>13</sup> and C<sup>14</sup> bonds. We shall report in this paper a preference for the evolution of C<sup>13</sup> as CO<sub>2</sub> when labeled urea is oxidized by chemical means.

The urea used to test discrimination in the carbon position was prepared by diluting, in alcoholic solution, a few crystals of high C<sup>14</sup> activity urea with Merck's Reagent

Grade urea. The solution was concentrated by evaporation of part of the alcohol, and the crystals that formed on cooling the solution were collected, washed with acetone, and dried. A part of the product was converted to xanthidrol ureide (9), giving a compound with one labeled carbon position as indicated in the formula above. The urea employed to determine discrimination in the carbon isotope was prepared in a similar manner, except that it was crystallized three times from alcohol. Further to assure the absence of radiocarbon not present as urea, a portion of the twice-recrystallized material was converted to urea nitrate (4).

The wet oxidations of all compounds with the Van Slyke-Folch mixture were carried out using the apparatus of Lindenbaum, Schubert, and Armstrong (6). For the fractional collections of the evolved CO<sub>2</sub> this apparatus was modified so that, when a part of the CO<sub>2</sub> had been collected in barium hydroxide solution, the stream of gas could be diverted, by turning a stopcock, into another receiver also containing barium hydroxide solution. In the majority of trials an effort was made to collect approximately half the evolved CO<sub>2</sub> as judged by the amount of precipitated barium carbonate, in each of the two receivers. However, Table 1 gives the results of one experiment in which the CO<sub>2</sub> was collected in 6 fractions. Owing to the vigor of the reaction of the acid-chromic acid oxidizing fluid with xanthidrol ureide, it was necessary to add the digestion fluid dropwise at a slow rate to the ureide contained in the evacuated apparatus. Only after the initial vigorous reaction had subsided was heat applied to the reaction thimble.

The dry combustions were carried out by using an ordinary microcombustion furnace, arranged in the manner described by Rittenberg (10), which allowed the emerging gas stream to bubble through barium hydroxide solution. By diverting the gas stream, two or more fractions of barium carbonate were obtained.

The barium carbonate was collected and its radioactivity determined by a previously described method (1,2). A majority of the precipitates exceeded "infinite thickness." In those cases in which the precipitate was of less than saturation thickness, the measured radioactivity was calculated to that at saturation thickness by use of a factor derived from an empirically determined self-absorption curve for C<sup>14</sup> β rays (2,4). All radioactivity measurements shown in a given table have been made comparable by use of a uranium standard.

Table 1 presents the data obtained from a wet and dry fractional collection combustion of xanthidrol ureide. A number of similar experiments have given results that are in agreement with those cited. In the case of wet oxidation, it is seen that the first fractions of the collected CO<sub>2</sub> contained far less C<sup>14</sup> than the later fractions. The first fractions were thus derived mainly from the unlabeled or xanthidrol residue carbons, whereas the later fractions contained most of the carbon from the urea residue. The results of the experiment in which the evolved CO<sub>2</sub> was collected in 6 successive fractions afford a striking demonstration of the relative slowness of conversion, by wet oxidation, of the carbon of the urea residue of xanthidrol ureide to CO<sub>2</sub>.

TABLE 2  
DISCRIMINATION BETWEEN ISOTOPES OF CARBON ON WET  
OXIDATION OF UREA AND UREA NITRATE

Material	Comb. No.	Carbon found, Fractions 1 and 2	Partition total carbon* Fraction 2 Fraction 1	C <sup>14</sup> assay
Urea	1	100.40	0.80	1.103
	2	99.75	2.50	1.147
	3	100.40	3.27	1.194
Urea nitrate	1	101.13	0.80	1.035
	2	101.44	1.37	1.142

\* Ratio of weights and hence of carbon contents of fractions.

The results of the dry combustions, in contrast to those of the wet oxidations, showed a preponderance of the labeled carbon in the first fractions, indicating a relatively earlier conversion of the urea residue carbon to CO<sub>2</sub> than of some of the xanthidrol residue carbons.

Table 2 presents representative data obtained on the fractional wet combustion of C<sup>14</sup>-labeled urea and urea nitrate. The radioactivity assays are shown as a ratio. The statistical deviation of the counts does not exceed 0.52% of the net sample count.

The results shown in Table 1 make it clear that it is necessary to oxidize completely xanthidrol ureide and to collect completely the evolved CO<sub>2</sub>, if reproducible results are to be obtained on C<sup>14</sup> assay of barium carbonate derived from this compound by wet oxidation. Since the C<sup>14</sup> is present in the last portion of the CO<sub>2</sub> to be evolved, undetectably small losses of carbon from this fraction would cause large errors in the C<sup>14</sup> assay. Such circumstances were undoubtedly the cause of the erratic results that we noted in the examination of the xanthidrol ureide prepared from urine referred to in the introduction. Concordant results with the synthetic xanthidrol ureide were obtained only when the reaction mixture was heated until the appearance of SO<sub>2</sub> (about 8 min) and the collection of the evolved CO<sub>2</sub> prolonged to at least 20 min following the end of the heating period.

Failure to collect completely the CO<sub>2</sub> formed by dry oxidation of xanthidrol ureide would likewise be expected to produce large discrepancies in C<sup>14</sup> assay, the effect on the specific activity of the barium carbonate being determined by whether the loss occurs from the first or from later portions of the evolved CO<sub>2</sub>. In fact, we had found already the counts of thick samples of barium carbonate derived in this manner from the ureide prepared from urine to vary from 215 ± 2.9 to 257 ± 2.4 cpm.

It is possible, in the case of wet combustion, that xanthidrol ureide is first hydrolyzed to xanthidrol and urea, and that the former product is more easily oxidized than the latter. Some support for this viewpoint was obtained from the observation that free xanthidrol, like xanthidrol ureide, begins to react with vigor at room temperature with the combustion fluid, whereas urea alone in the reaction mixture requires heat for initiation of the reaction and the evolution of CO<sub>2</sub>. Also related to this point are the results of a fractional wet combustion of a mixture of 2 moles of xanthidrol and 1 mole of labeled

urea, which gave the following specific activities of barium carbonate: Fraction 1 (containing 40.4% of the total carbon), 0.6; Fraction 2 (containing 59.2% of the total carbon), 444.5.

The data presented in Table 2 demonstrate that the CO<sub>2</sub> formed late in the chemical oxidation of C<sup>14</sup>-labeled urea is relatively richer in the label than that which is first produced. Since comparable results were obtained with urea nitrate, added assurance is given that the results were not due to the presence of a radioactive contaminant more resistant than urea to oxidation. Because of the variation of the weights of the 2 fractions among the several combustions and other uncontrolled variations affecting the reaction, no precise statement can be made as to the magnitude of this form of isotope discrimination. However, it appears from an inspection of the results that the last half of the evolved CO<sub>2</sub> contained about 10% more C<sup>14</sup> than the first half.

It is possible that other isotopic carbon-labeled compounds may exhibit to a degree behaviors similar to that of xanthidrol ureide and urea on oxidation. On this account an important precaution should be observed in the conversion of compounds labeled with either C<sup>14</sup> or C<sup>13</sup> to CO<sub>2</sub> when this compound is to be used for isotopic carbon assay. Because of the probable different rates of oxidation of carbons of an organic compound, and isotopic discrimination of identical positions of carbon atoms in a compound, care should be taken to achieve complete oxidation and mixing of the resulting CO<sub>2</sub> before removal of samples for carbon analysis. Dependence should not be placed on a sample of the evolved CO<sub>2</sub> as representative of the C<sup>14</sup> specific activity or the C<sup>13</sup> content of the material. The whole of the sample should be burned, and the CO<sub>2</sub> collected completely and precipitated. If an aliquot of the CO<sub>2</sub> is to be used, opportunity should be afforded for mixing before the aliquot is taken.

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## New Tests for the *Nicotiana* Alkaloids, Nornicotine and Anabasine<sup>1</sup>

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We wish to give preliminary accounts of two new color tests for *Nicotiana* alkaloids, one for nornicotine and anabasine, and another for nornicotine. We find that nicotine fails to give similar color reactions in both tests.

A solution of quinhydrone (5 g in 100 ml of ethyl alcohol) will react with nor nicotine and anabasine at pH of 7 (phosphate buffer) to give a cherry-red solution. Five-hundredths g of either nor nicotine or anabasine in 10 ml of buffer solution and 10 ml of quinhydrone solution will give immediately a deep cherry-red solution. A similar quantity of nicotine will give almost no color change in the original quinhydrone solution.

The second test (for normicotine) uses as color-producing reagents 1,3-di-ketohydrindene, *p*-hydroxybenzoic acid, acetone, and di-isopropyl ketone. Normicotine reacts with these reagents to give a violet color, which has a maximum absorption peak at approximately 540  $m\mu$ . This test is extremely sensitive. Three hundred sixty-three  $\gamma$  of normicotine in 5 ml of acetone, plus 15 ml of di-isopropyl ketone, 2 ml of 2% *p*-hydroxybenzoic acid in di-isopropyl ketone, and 2 ml of .3% solution of 1,3-di-ketohydrindene in di-isopropyl ketone gives a reading of 384 at 540  $m\mu$  on the Klett-Summerson colorimeter within 60 min after the start of the reaction. The same quantity of nicotine or anabasine does not give this violet color under the same conditions.

We are continuing work on these two tests.

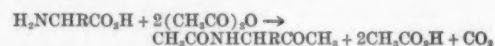
<sup>1</sup> Report of a study under the Research and Marketing Act of 1946.

### Mechanism of the Dakin and West Reaction

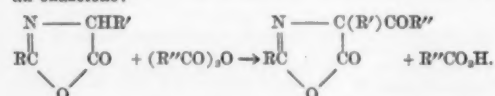
J. W. Cornforth and D. F. Elliott

*National Institute for Medical Research,  
London, England*

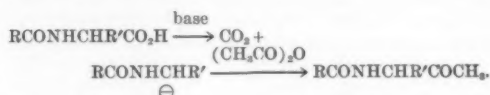
Dakin and West (2) showed that many  $\alpha$ -amino acids give  $\alpha$ -acetamidoalkyl methyl ketones and carbon dioxide when heated with pyridine and acetic anhydride at 100° C:



It is our view that in this synthesis the new carbon-carbon link is formed by the base-catalyzed acylation of an oxazolone:



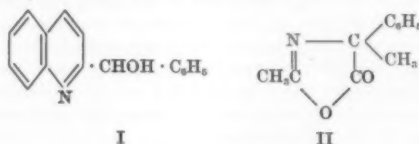
This reaction mechanism is cited in full detail by Wiley (5), who nevertheless rejects it in favor of an initial base-catalyzed decarboxylation, the carbanion then reacting with the acetic anhydride or other carbonyl component to give the final product:



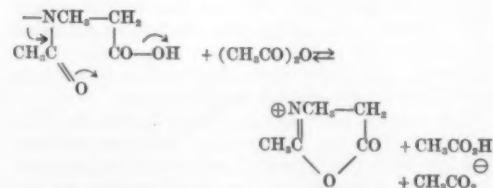
Wiley's rejection of the oxazolone mechanism is based on his observation that *N*-acetylsarcosine, which he says cannot form an oxazolone, can be converted under the usual conditions to *N*-methylacetamidoacetone.

It should first of all be mentioned that the idea of "decarboxylation as a source of reactive carbanions" is not novel, having been put forward some time ago (4) to account for the behavior of quinaldinic acid when decarboxylated in the presence of a carbonyl compound: the product with benzaldehyde, for example, is phenyl 2-quinolyl carbinol (I).

We find no decarboxylation of acetylglycine to occur on boiling with pyridine (or with a mixture of pyridine and benzaldehyde). This fact alone makes Wiley's mechanism unacceptable without modification. In addition, Dakin and West (8) found that  $\alpha$ -aminohydratropic acid affords no carbon dioxide (and no ketone) when heated with acetic anhydride and pyridine. This is readily understood on the basis of the oxazolone mechanism, for no hydrogen atom replaceable by acetyl is available in the oxazolone (II); but the fact is not accommodated by Wiley's scheme, as *N*-acetylaminohydratropic acid could give a carbanion by decarboxylation.



Wiley's result with acetylsarcosine can be explained by assuming the transitory formation of an oxazonium cation:



Acetylation, ring-opening, and decarboxylation are then assumed to follow in the usual way. We believe that the condensation of *N*-benzoylserosine with benzaldehyde to give  $\alpha$ -(*N*-methylbenzamido)cinnamic acid (*S*) proceeds by way of an analogous intermediate.

It is interesting that Dakin and West (2) reported that sarcosine itself gave little carbon dioxide and no



identifiable ketone on heating with pyridine and acetic anhydride. The contrast between this and the result with *N*-acetylsarcosine is perhaps due to the presence of additional acetic acid (arising from the initial acetylation) in the reaction mixture from sarcosine. Acetic acid has been shown (1) to have a deleterious effect on the condensation of hippuric acid with acetic anhydride in the presence of pyridine.

We regard the Dakin and West reaction as a special case of the Erlenmeyer synthesis of oxazolones; we hope to have shown here that Wiley's observation is consistent with this view and does not require a separate hypothesis.

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## Electronic Radiography by Transmission Using Radioactive Monolayers

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Herein is described a method of electronic radiography by transmission which may be compared with the photographic printing process, with the difference that electrons, or  $\alpha$  particles, replace the light. The specimen is placed between, and in intimate contact with, a uniformly radiating source on one side and a photographic plate on the other. This method was made possible by the preparation of homogeneously radiating sources in the form of mono- or multilayers of molecules tagged with radioactive isotopes (1). The layers were prepared by using the technique developed by Langmuir and Blodgett (2) for "built-up" films.

A  $\beta$ -emitting source can be prepared by spreading  $C^{14}$  labeled stearic acid on the surface of an aqueous solution ( $10^{-4}$  M  $CaCl_2$ ,  $10^{-3}$  M  $KHCO_3$ ) and transferring the monomolecular film of calcium stearate to a solid substratum by dipping a plate once or several times through the surface. In this way a mica plate of a few square centimeters in area can be covered on both sides homogeneously with one or several monolayers of radioactive calcium stearate. By cleaving the mica sheet, two sources buttered with radioactive material on only one side can be prepared. It is obvious that this method can be used for the preparation of homogeneous sources of  $\alpha$ ,  $\beta$ , or  $\gamma$  radiation, with wide variation in penetrating power, by incorporating various radioactive elements in the monolayers—for instance, by the use of radium,  $Sr^{90}$ ,  $Ca^{45}$  stearate.

The picture of a thin specimen in the  $\beta$  light of  $C^{14}$  can be prepared by enclosing the specimen in a printing frame between the radioactive layer and a photographic emulsion

(no-screen x-ray film or industrial x-ray film, Type M, from Eastman Kodak Company), as demonstrated in Fig. 1. An example of the results of this method is given in the picture of an unscaled wing of a butterfly reproduced in Fig. 2.

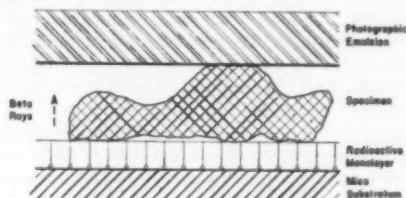


FIG. 1. Diagram of arrangement for electronic radiography by transmission (arbitrary measure).

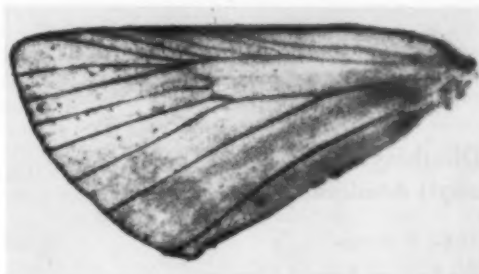


FIG. 2. Unscaled wing of butterfly depicted by electrons emitted from  $C^{14}$  ( $\times 5$ ).

These electron radiographs can be explained in the same way as images obtained with the electron microscope. In fact, the mean velocity of the electrons emitted from  $C^{14}$  corresponds to the velocity of the electrons in the usual electron microscopes (50 kv). The shades in the picture are determined by the product of density and thickness of the specimen. When this product surpasses a certain value for a given electron velocity, only the outlines of the specimen can be made visible.

Compared with the electron microscope, the contact method is limited in resolving power and in magnification. The electrons are emitted from the source in all directions with different velocities. Under these conditions the resolving power is a complex function with a variety of factors. Some of these are the distribution of the electron velocity in the  $\beta$  spectrum, the thickness in  $g/cm^2$  of the specimen and the photographic emulsion, and the grain size of the photographic material. From the separation of two points in Fig. 2 a resolving power of about 10–20  $\mu$  was estimated. Under these conditions the useful magnification cannot surpass the factor 10.

The contact method, however, has some marked peculiarities that may recommend its use in special cases. The wide variety of electron velocities from 0.015 to some million ev, which can easily be applied by changing the radiating element in the source, offers an inexpensive possibility (no machine) for studies of transmission of electrons over a considerable range. In this regard beta-

graphs of specimens with greater "thickness" will be of special interest.

Work is in progress to accomplish electron radiography by transmission on a quantitative basis. The uniform intensity of the sources was measured by the methods of absolute  $\beta$ -counting. These values can be compared with the electron intensities in the betagraph, determined with a microdensitometer. The results represent a measure for the absorption of electrons of a given mean velocity in small areas (limit, 30  $\mu$  diameter) which is related to the "thickness" of the structure of the specimen.

The application of  $\alpha$ -emitting monolayers (radium, polonium, plutonium) opens up new possibilities for studies of specimens in  $\alpha$  light. Pictures of butterfly wings depicted in the radiation from a radium stearate source show about the same shades as the betagraph in Fig. 2.

Descriptions of other applications of radioactive monomolecular films will appear elsewhere.

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## Dicarboxylic Acid Bis-( $\beta$ -Tertiaryaminoalkyl) Amides as Curare Substitutes

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A series of bis-( $\beta$ -dimethylaminoethyl) esters of dicarboxylic acids was recently reported (1) to possess powerful curarelike activity. Concurrently with the esters, a group of bis-( $\beta$ -tertiaryaminoalkyl) amides of the dicarboxylic acids was prepared and examined for curariform action.

The bis-amides were obtained in excellent yields by brief refluxing of a slight excess of the unsymmetrical disubstituted ethylene diamines with the dimethyl or diethyl esters of the dicarboxylic acids. In most cases the bis-amides were crystalline solids readily recrystallized from organic solvents. The bis-tertiary amino amides were transformed into bis-quaternary ammonium salts by refluxing in methanol solution with an excess of the appropriate alkyl halide, most commonly methyl or ethyl iodide.

Examples of the types of products made are: bis-dimethylaminoethyl oxamide (mp, 123°-124°; calcd.: C, 52.1; H, 9.6. Found: C, 52.1; H, 9.6); its bis-methiodide (mp, 288°-290°; calcd.: C, 28.0; H, 5.5. Found: C, 28.2; H, 5.5); bis-dimethylaminoethyl succinamide (mp, 134°-135°; calcd.: C, 55.8; H, 10.1. Found: C, 55.6; H, 9.9); its bis-methiodide (mp, 251°-252°; calcd.: C, 31.0; H, 5.9. Found: C, 31.1; H, 5.9); its bis-ethiodide (mp, 189°-190°; calcd.: C, 33.7; H, 6.4. Found: C, 33.7; H, 6.1); bis-diethylaminoethyl adipamide bis-methiodide (mp, 134°-135°; calcd.: C, 38.4; H, 7.1. Found: C, 38.9; H, 6.8); bis-morpholinoethyl malonamide

(mp, 127°-128°; calcd.: C, 54.8; H, 8.6. Found: C, 54.8; H, 8.4); and its bis-methiodide (mp, 153°-154°; calcd.: C, 33.3; H, 5.6. Found: C, 33.7; H, 5.4).

Interestingly, both the bis-tertiary amino amides and the derived quaternary salts were relatively devoid of curarelike activity, requiring huge doses to produce any perceptible block of neuromuscular transmission in the cat. However, both in the tertiary and quaternary form these compounds have been found to possess the remarkable ability, anticholinesteraselike, to prolong the duration of the block produced in the cat by the bis-esters (1) as much as four or five times. Details of the pharmacological results will be published elsewhere by E. J. de Beer and J. C. Castillo of these laboratories. Further work along these lines will be reported later.

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## The Enzymatic Dehydrogenation of Estradiol to Estrone<sup>1</sup>

Joseph A. Ledogar and Howard W. Jones, Jr.<sup>2</sup>

*Department of Gynecology, The Johns Hopkins University, Baltimore, Maryland*

An enzyme system that catalyzes the conversion of  $\alpha$ -estradiol to estrone, *in vitro*, was demonstrated by using a purified protein fraction of beef liver and rat tissue homogenates as enzyme sources.

A 2-mg sample of a crudely purified preparation from the acetone-insoluble, water-soluble fraction of beef liver was tested for ketosteroid and found to be negative (1). A 5-mg sample of crystalline  $\alpha$ -estradiol<sup>3</sup> was likewise negative.

Five mg of the estradiol was added to 0.2 mg of the purified beef liver preparation in 20 ml of water and incubated for 12 hr under conditions previously found to be within the range of maximal enzymatic activity. Twenty ml of a 0.1% solution of 2-hydroxy-3-naphthoic acid hydrazide, containing 50% ethyl alcohol and 5% acetic acid, was stirred into the mixture, brought to boiling, and cooled to room temperature. The yellow precipitate formed was separated from both the excess hydrazide and any estradiol present by centrifugation, repeatedly washed with 50% ethyl alcohol, and refluxed with pyruvic acid for 30 min. Distilled water was added to saturation, and a white crystalline precipitate was formed on cooling (3). The crystals were purified by repeated washings with warm 5% sodium bicarbonate solution and warm distilled water. After drying in air, the crystals were examined microscopically and found to be colorless plates similar in form to estrone. The mp was 252°-254° C. When some of the crystals were mixed with a known sample of crystalline estrone<sup>3</sup> (mp 253°-

<sup>1</sup> Aided in part by a grant from the Maryland Division, American Cancer Society, to R. W. TeLinde and Howard W. Jones, Jr.

<sup>2</sup> Leslie Hellerman gave valued assistance in this work.

<sup>3</sup> Supplied by courtesy of Schering Corporation.

255° C), the mp rose to 253°–254° C. The ketosteroid test was positive. Positive rat tests for estrogenic activity, as estimated by increases in uterine weight ( $\%$ ), were obtained by as little as 32  $\mu$ g, which resulted in uterine weight increases from an average of 25 mg to 82.5 mg for rats of 36.3 gm average weight. The yield estimated on the basis of solubility in ethyl alcohol was 2.2 mg.

To establish the activity of the liver preparation as enzymatic the following tests were performed:

1. Inactivation by boiling: Fifteen test tubes, each containing 0.1 mg of the liver preparation in 20 ml of distilled water, were used. Tubes 1–5 were boiled 15 min and cooled; ketosteroid tests were negative. Two mg of crystalline  $\alpha$ -estradiol was added to tube 6–10 and incubated 6 hr at 37° C; all contents were strongly positive for ketosteroid. Tubes 11–15 were boiled 15 min, 2 mg of crystalline  $\alpha$ -estradiol was added, and the tubes were incubated 6 hr at 37° C; all ketosteroid tests were negative. Five tubes containing 2 mg crystalline  $\alpha$ -estradiol only in 20 ml of distilled water were incubated 6 hr at 37° C; all ketosteroid tests were negative.

2. Inactivation by silver nitrate or bichloride of mercury: Nine tubes, each containing 0.1 mg of the liver preparation in 20 ml of distilled water, were used. To tubes 1–3, 0.034 g  $\text{AgNO}_3$  was added. To tubes 4–6, 0.0544 g  $\text{HgCl}_2$  was added. Tubes 7–9 were used as controls. To all tubes 2 mg of crystalline  $\alpha$ -estradiol was added, and, after 6 hr incubation at 37° C, each was tested for ketosteroid; tubes 1–3 and 4–6 were negative, and 7–9 were strongly positive.

3. Rate of production of ketosteroid, when concentration of enzyme was small as contrasted to that of the substrate, was shown to be constant (Fig. 1).

4. Variation of activity with temperature: Two mg  $\alpha$ -estradiol and 0.1 mg liver preparation in 20 ml distilled water were incubated 6 hr at 2-degree intervals from 29°–45° C. Maximal ketosteroid production, estimated colorimetrically, occurred between 33°–35° C, approximately 50% at 31° and 37°, 25% at 29° and 39°, and 10% at 45° C.

5. Influence of pH on activity: Two mg  $\alpha$ -estradiol and 0.1 mg liver preparation were incubated at 35° C with 20 ml of 0.1 *N* isoelectric buffer solutions from pH 4.8 to 8.8. Maximal ketosteroid production occurred between pH 6.8 and 8.0, approximately 50% at 6.2 and 8.8, 15% at 4.8.

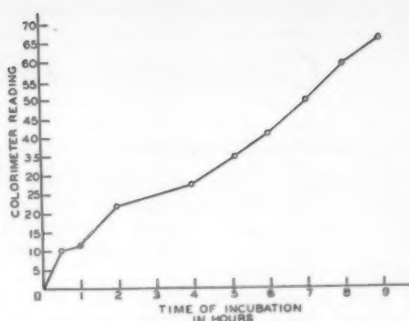


FIG. 1. Two mg crystalline  $\alpha$ -estradiol, 0.02 mg liver preparation, 20 ml distilled water/tube were incubated at 37° C; 1 tube/hr was quantitatively tested for ketosteroid, using a Klett photoelectric colorimeter and #54 filter. Time of incubation in hr is plotted against colorimeter readings.

The enzyme was shown to be a dehydrogenase by the following test: Six small flasks, each containing 2 mg crystalline  $\alpha$ -estradiol and 0.2 mg liver preparation in 10 ml 0.1 *N* citrate-phosphate buffer pH 7, were used. To flasks 1–3 was added 0.5 ml 1% methylene blue. Flasks 4–6 were controls. Anaerobic incubation under nitrogen was performed for 3 days at 37° C, then each was tested for ketosteroid; 1–3 were positive and 4–6 negative. Methylene blue was completely decolorized in flasks 1–3.

Inhibition experiments showed the enzyme system was not inhibited by cyanide *M*/500, or epinephrine 1:1000, and only partially (approximately 2/3) inhibited by ethyl alcohol 70%–80%.

Crystalline  $\alpha$ -estradiol was incubated with rat tissue homogenates, and tests for ketosteroid were performed. Positive results were obtained with liver, kidney, breasts, and testis, but those with uterus, ovary, and adrenal were negative, as were the controls.

Attempts at further purification will be made to demonstrate possible substrate specificity of the enzyme.

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## Comments and Communications

### The Payment of the Learned Man

Dr. E. Bodewig, a German mathematician now living in Holland, has been reviewing papers for *Mathematical Reviews* for several years. Recently he resigned as a reviewer, and in reply to my letter of regret he sent the enclosed letter of explanation.

The letter was written in German, and I have translated it rather freely. Dr. Bodewig has given me permission to have it published and suggests that it should be introduced by the following quotation from Wagner's *Siegfried*: "After vain distant things you sought, but what was found close at hand, what you needed, that did not enter your head."

R. P. BOAS, JR.

Executive Editor, *Mathematical Reviews*  
Brown University, Providence, Rhode Island

#### DEAR PROFESSOR BOAS:

After long consideration and many years of observation, I have made up my mind to withdraw from scientific activity. I have cut one thread after another and, like Gulliver, I am abandoning the island of the mathematicians. Consequently, I must give up my collaboration with *Mathematical Reviews*. When one has devoted so many years to mathematics, one does not lightly abandon it. Let me briefly explain my reasons.

Nowhere in the world do the scholar and the learned man understand how to secure the position and the pay that they deserve. This has surprised me for many years, all the more because, on account of my financial independence, I could to a certain extent observe the situation from the outside and, in addition, because I am one of the few mathematicians who have carried out and published theoretical work in psychology and finance and have had the necessary practical experience on the stock exchange. And I must say that I am astonished that the low pay of the learned man has never yet been the subject of an investigation. It should be a task for the United Nations to look into it sometime, just as they have done, with endless discussions, with the problem of labor and the problem of colonial peoples.

What lawyer would be satisfied with the pay of a scholar? For a simple routine letter requiring no technical knowledge he demands 25-50 gulden in Holland (in Germany, as many marks, and in the U.S.A., I suppose, as many dollars). For a routine petition to the authorities he demands 120-250 gulden (marks, dollars), and that is a quarter of an hour's work. For small jobs he demands 200 gulden in advance before he begins to work at all. Later on he gets easily 500 gulden. If a lawyer had to do as much work and as much preliminary study as I (or anyone else) had to do, for example, in reviewing the papers of von Neumann or Reicheneder, he would demand 1,000 gulden and get it and be upheld by any court. What do I or anyone else get for this? Nothing.

If I had received for each review the fee that a lawyer would have received for the same time and mental effort, I would have received 100-1,000 gulden for each review, and altogether about 30,000 gulden. What did I get? Nothing.

Let us take another profession, chemistry, for example. An acquaintance of mine gets 1,500 gulden for an extensive chemical analysis, and nobody has ever considered this excessive. If I had received only 500 gulden for each of my 150 reviews, this would have come to 75,000 gulden. What did I get? Nothing.

Let us take the chief physician in a hospital. In the morning he goes through his clinic where there are 100 patients. He speaks a few words to some of them but says nothing at all to most. The whole thing takes a quarter of an hour. But each patient pays him 1-10 gulden. That amounts altogether to at least 150 gulden, probably more. If I had received 150 gulden for each quarter of an hour's work on my 150 reviews . . . (I don't want to count it up).

Let us take an ordinary doctor. For each appointment he gets 3-10 gulden. A prominent doctor gets many times as much. That amounts to an income of some 500 gulden a day.

I heard of a camp for German prisoners of war in Australia. The prisoners were allowed to work and were all paid. Well paid! But there were also teachers and professors there, who were giving valuable instruction to the other prisoners. These teachers were the only ones who were not paid for their work. In fact, at the end of the class they had to sweep out the classroom, since the students didn't do it.

Do I have to remind you of the disgraceful fact that a bookseller gets 30% commission, often 40%, for each book he sells, he who often cannot read a single line of the book? While the learned man who wrote the book gets 10%? (Of course I am aware that a bookseller has certain expenses.) Do I have to remind you of the disgraceful fact that the compositor often gets more pay for setting up a book than the author gets for writing it? Do I have to remind you that the compositor gets his pay at once, whereas the author has to wait for an annual accounting?

I wrote a book on *Numerical Methods* in a year and a half, working 5-10 hours a day. It was translated in the U. S. When the contract was drawn up, it turned out that I was to get about \$350 (and the translator the same amount). And this in a field where one can say that no book at all existed before. Afterwards the publishers wanted to make even these conditions worse in underhanded ways. Then I canceled the whole contract on the ground of violations of its terms. What lawyer, doctor, or chemist would work for a year and a half or two years for \$350? Are we scholars only for philanthropic purposes?

*Mathematical Reviews* can pay the compositor, printer, paper manufacturer, paper dealer, etc. Only the scholars who write the reviews get nothing. Nobody in the world would think of asking a compositor, printer, etc., to work for nothing. Only among scholars is this taken for granted. After all, why?

I have mentioned only the professions which are closest to us: medicine, chemistry, law, etc. I have not said anything about businessmen, who frequently make 6 million gulden in a single morning by making two or three telephone calls (I have a perfectly definite case in mind).

But for their poor pay the scholars have to thank not only the "world" and not only their own awkwardness, but also their colleagues. For example, Professor X invited me to take a position at the Mathematical Center at Amsterdam—for 300 gulden a month. I wrote to him that for that he could get a plumber. It is too bad that at the time I had not seen a newspaper advertisement for nurses in an insane asylum at 3,300 gulden a year with half room and board. Otherwise I would have recommended a nurse from the insane asylum to my "colleague," (even though she would have received rather less pay at the Mathematical Center). It is also too bad that I had not seen my twelve-year-old son's arithmetic problem, where ten bricklayers got 10 gulden per man per day. Otherwise I would have recommended a bricklayer to my "colleague" for the Mathematical Center. Another professor wanted me to give lectures (free, naturally). I answered him similarly.

A German professor invited me to give a lecture at his university. I did it but discovered afterwards, to my great surprise, that with childlike innocence he had never thought of an honorarium. I had to pay all the expenses of the long trip out of my own pocket. No plumber in the world would have expected as much from me as this "colleague."

A scholar in the U. S. asked me, in the name of his institution, three or four questions about a problem with which his institution expected to be seriously concerned in the next few years. Instead of answering the questions, I asked him for a guarantee of \$2,000 (a lawyer would have asked much more). After that he didn't seem to need the answers.

A German professor asked me to take over a course of lectures, in one of the most difficult of all subjects, for a semester. He added that he did not have any idea of how much I would be paid, since he was "not fully informed." (Now, in that case, he should become better informed and then ask again.) What workman in the world would take on a helper without telling him his wages?

I must decline to go into the psychological reasons why the "world" pays the scholars so poorly, and why the scholars themselves are satisfied with this poor pay, and why, finally, the scholars treat each other so badly. Briefly, it comes down to this, that every intelligence is only partial; that the highest form of individuality—i.e., the highest development of the mind—is possible only in a limited domain, and that everything that lies outside this domain is judged with decreased ability. If I were not educated otherwise through years of study of the stock exchange, I should be as unworldly as the others.

"Naturally" one does not use his science for making money. (It would be terrible if a scholar did what everybody else takes for granted.) But the exploitation of the scholar is one of the worst in the world. It is the modern social problem! Nobody bothers about it, not even the scholars themselves. It would be a job for the United Nations, but they don't do anything either.

One will hardly be able to influence the scholars to look after their own material interests. Under the circumstances I can only act for myself. I don't like the rules of the game and I won't play any more. I want my work to be well paid, like that of a doctor, a chemist, or a lawyer. If the world won't do that, I shall not work any more for the "Society of Mankind." I strike. (But sometime the U. N. should take up the rate of pay of the rest of the scholars who are still working. The scholars would agree with me there.)

Sincerely yours,  
E. BODEWIG

### Sphagnum Moss and Egg Yolk as Food for Anuran Tadpoles

Different kinds of food have been used by various investigators to rear anuran tadpoles in the laboratory. Algae, liverworts, lettuce, or spinach, supplemented by beef liver, powdered egg yolk, or a dry pulverized mixture of whole-wheat flour and bacto-beef extract, have been tried (Rugh, R. *Experimental Embryology*. Minneapolis: Burgess Publ., 1948). When fresh liver is used, putrefaction occurs quickly. Unless the water is changed frequently and the decayed liver removed, the tadpoles will die as a result of pollution of the water. Briggs and Davidson (*J. Exp. Zool.*, 90, 401 [1940]) found that spinach-fed tadpoles developed most rapidly but produced kidney stones. Although boiled lettuce is better food than spinach, it also decays in a short time, especially at warm room temperatures.

For the past two years, sphagnum moss<sup>1</sup> supplemented by egg yolk has been used by the writer to rear different species of anuran tadpoles in his laboratory. The result has been satisfactory. Under laboratory conditions metamorphosis took place about 70 days after insemination. No stones were found in the kidneys of either the tadpoles or the metamorphosed young. The sphagnum moss can be stored dry in the laboratory to be used as needed. The egg yolk is prepared by hard boiling the eggs, separating the yolk from the white, and then crushing it into small lumps and drying it. A few small lumps of egg yolk are fed at a time, as too much left in the medium will also pollute the water. In the summer, the water needs to be changed twice a week, whereas in the winter once every 5 to 7 days is sufficient.

Sphagnum moss decomposes slowly, forming acid, and the acidity of the water in turn reduces the growth of bacteria. The pH of tap water in our laboratory has been found as high as 10. If a large amount of sphagnum moss is soaked in it for a day, the pH will be low-

<sup>1</sup> Dry sphagnum moss can be purchased from seed stores, or from E. G. Steinhilber Co., Oshkosh, Wis., at about 50 cents per pound.



ered to about 5.4, but tadpoles will survive even at this low pH. The pH is somewhat higher if less sphagnum moss is added. Several of the tadpole cultures containing sphagnum moss in tap water have been tested, and the pH was found to vary from 6.2 to 6.9. Therefore, in using sphagnum moss as food, not only is bacterial growth reduced, but also laboratory tap water can be used without any harmful effect on the tadpoles. This method of rearing tadpoles is economical as well as time-saving.

HAN-PO TING

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### Oaths and Affidavits

Dr. Grundfest omitted from his discussion "On Political Oaths and Affidavits" in *SCIENCE* for July 21, 1950, the core of the problem, namely, the criminal aspects of the Communist Party. He repeatedly referred to political beliefs but said nothing about criminal beliefs. The word "Communist" carries a connotation of lawlessness that does not apply to our major political parties. For example, few professional Democrats and Republicans enter this country under false names or by means of untruthful affidavits.

I don't care about the politics of my doctor or my lawyer, but I do not wish either one to be a member of, or in sympathy with, a criminal organization. At the same time I see little merit in miscellaneous "oaths and affidavits." It doesn't do much good to ask a man if he is a criminal or if he associates with criminals.

P. W. MERRILL

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### Basic Processes of Erosion

We who are interested in the conservation of our soil resources appreciate your article "Soil Erosion by Rainstorms," by W. D. Ellison (*Science*, 111, 245 [1950]). The article should be quite beneficial in disseminating information on the basic processes causing erosion.

Two faulty statements were made, however, that should be corrected. These statements appear on page 246, column 2, last two paragraphs as follows: "However, these experimenters apparently did not recognize splash erosion as an important independent erosion process. The first known reports on splash erosion were made by the writer (3, 4, 5)."

Much of Mr. Laws' work on raindrops and erosion has remained unpublished, as he left Soil Conservation Service research for work more closely connected with our war efforts. As one closely associated with Mr. Laws and the work on effects of raindrops, I can definitely state that not only did Mr. Laws recognize the importance of splash erosion, but it was also recognized by the men in charge of this research (Donald A. Parsons and Howard L. Cook).

Mr. Laws not only recognized the significance of

splashes but photographed the splashes and splashed soil (*Agr. Eng.* 21, 432 [1940], Fig. 3, B and C, left, entitled: B. Just after striking. C. The air is filled with flying soil particles).

In addition, I would like to quote from the *S.C.S. Research Project Monthly Report* for May, 1941. (Note items 1a and 2.)

A few of the phenomena of general interest that have been observed, or that are deducible from the observations, are outlined below.

#### 1. Raindrops impinging upon soil cause:

- (a) *Splashing* which results in large quantities of soil and water being transported from one place to another. It is easy to reason that on sloping land, the distance of travel of these splashes is greater down the slope than up; also, soil splashed into nearby rapidly flowing water becomes highly susceptible to being carried away.
- (b) *Loosening* of the soil particles at the surface, giving the run-off waters an opportunity to act upon them.
- (c) *Turbulence* in the run-off water which aids in the maintenance of the soil particles in suspension.
- (d) *Shattering* or breaking down of the soil aggregates into more easily erodible material.
- (e) *Rearranging* of the particles at the ground surface which serves to reduce the infiltration rate.
- (f) *Puddling and tamping* which tends to alter the soil structure near the surface, resulting in a thin compacted layer which further reduces the infiltration rate and thereby increases the run-off rate and rate of soil erosion. As rearranging, puddling and tamping progress, the erodibility of the surface decreases.
- (g) *Leveling*, or localized erosion and deposition, which reduces depression storage and results in greater amounts of run-off and soil loss. Leveling is a result of several of the primary actions.

2. Because of splashes, a large part of the run-off occurring from each small area of bare soil consists of water and soil transported to that area by means of splashes from the adjacent areas. Consequently, the soil and water losses by run-off from any small area of bare soil are less if the area is bounded by areas from which splashing does not occur. It was observed that a large part of soil and water losses from a 2-foot square plot of soil subjected to an erosive rain took place through the medium of splashes rather than through the medium of run-off. This phenomenon is implicitly involved in the balk method of farming.

3. In some of the tests the soil surface was covered for brief periods with a roof that shielded the soil from direct hits by the raindrops, but drained their water gently onto the soil. Under this condition, overland flow was occurring without rainfall impact effects. When the roof was removed, the same magnitude of flow existed but with disturbances caused by the striking raindrops. A run-off rate of 3 inches per hour was observed to produce no erosion when the roof protected the soil surface. When the roof was suddenly removed, the soil concentration jumped to 2 percent by weight of the run-off.

4. Experiments of this type have wide application because they show individual processes, uncomplicated by external factors. Thus, one practical value of the above experiment is to demonstrate the essential function of soil covers. It is evident that any cover, whether it be metal, stone, vegetation or plant residues, that protects the soil surface from rainfall impact, will reduce soil losses materially.

5. Depending upon plot conditions, the results also show that there is a certain rate of overland flow below which erosion will not occur from the action of run-off alone. Although in these experiments the bed material was an agricultural soil and the depths of flow were only a few hundredths of an inch, this result should not be surprising, since many experimenters concerned with the movement of bed load in open channels have determined that for any

given bed material and flow condition there exists a critical velocity below which scour does not occur.

6. With these facts in mind, the following important paradox in the mechanics of erosion can be stated: *The velocity of non-erosive flow affects erosion.* With the aid of the disturbances caused by beating rain, otherwise sub-critical or non-erosive flows do move soil and—just as in erosive flows—their velocity affects the erosive rate. It is easily observed that many particles raised from their resting places for a brief moment at raindrop impact, travel down slope. The distance of travel is undoubtedly dependent upon the velocity of run-off.

7. There is some evidence, obtained from mechanical analyses of the sediment load from two tests which differed in run-off rate, that variations in run-off rate and consequently velocity, affected the amount of the largest particles but not the finest. Thus, it may be concluded that a condition exists in these shallow "sheet" flows that is closely analogous to that reported as existing in streams. Here, as in rivers, the quantity of fine soil carried in suspension does not appear to be influenced greatly by the rate of run-off. On the other hand, the amount of larger particles which move as bed load appears to increase with in-

creasing flow velocity. If this be true, then insofar as the test conditions represent field conditions—and it is believed they do for an appreciable portion of most cultivated fields for most run-off periods—the erosive forces accompanying rainfall impact are solely responsible for the losses of the finer portion of the soil. And methods devised to reduce the velocity of overland flow, which do not protect the soil surface from rainfall impact or reduce the total quantity of run-off, will not effectively reduce the losses of this highly important finer portion of the soil which carries much of the fertility.

Finally, it appears that Mr. Ellison's reference (5) (*Sci. Mon.* 1940, 63, 241) is nonexistent.<sup>1</sup>

NORVAL L. STOLTENBERG

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<sup>1</sup>Ed. Note: This reference was erroneously recorded. The article in question starts on p. 241 of vol. 68, 1940, of *The Scientific Monthly*.

## Book Reviews

*Anatomy of the Dicotyledons: Leaves, Stem, and Wood in Relation to Taxonomy*, 2 vols. C. R. Metcalfe and L. Chalk. New York: Oxford Univ. Press, 1950. 1,500 pp. \$25.00 the set.

During a period when it seems that altogether too many botanists are wasting their time and effort in adding to an already marked superfluity of elementary botany texts, it is indeed refreshing when others demonstrate that they have a far better understanding of the real needs of the botanical sciences. The present book is a basic and truly monumental contribution toward a comprehensive knowledge of the vegetative organs of the Dicotyledons on a taxonomic basis.

The work is founded upon Solereder's *Systematic Anatomy of the Dicotyledons* and has the same chief aim—namely, to emphasize the taxonomic and phylogenetic values of anatomical characters—but the oft-repeated complaints against Solereder's treatise have been circumvented. The larger part of the book and the introduction are the work of the senior author, the junior one being responsible mainly for the descriptions of secondary woods. They were assisted by many other specialists.

The introduction is superb; every aspect of each subject treated, the pros and cons as advanced by various workers, have been fully discussed with admirable perspicacity.

Treatment of the families follows Bentham and Hooker in general, with the addition of those whose erection since their time has been generally recognized. Each family is begun with a terse summary concerning (1) general features and (2) wood anatomy, following which the leaf, axis, and root are discussed, together with paragraphs on ecological anatomy, anomalous structure, economic uses, and taxonomic notes. Roots are too briefly described and are omitted entirely for many families; in the re-

viewer's experience, these organs deserve more attention than most botanists seem to realize.

Factual errors are remarkably few. The reviewer checked numerous statements concerning plants of which slides were available but found only one inaccuracy. The leaf of *Petalonyx thurberi* (p. 669), said to be centric, actually is isobilateral, and the vascular tissue of the midrib consists entirely of lignified, pitted cells. Most of the errors concern geographical distribution, but many of these plainly were copied from sources which in turn were mistaken. As one instance, the citation for the distribution of the Saururaceae (p. 1127), which is given as Malayan, is apparently taken from Hutchinson's *Families of Flowering Plants*, yet the latter illustrates *Anemopsis californica* as representative of the family. All authors concerned should have observed that the specific epithet hardly refers to a Malayan region. No typographical errors have been noted, but one wonders why "g" is substituted for the "z" in Schizandraceae.

One specific criticism concerning morphological-taxonomic relationships is pertinent: the inclusion of *Trapa* in the Onagraceae (p. 664 *et seq.*). All the morphological and embryogenic evidence, which should have been noticed by the authors, excludes that genus from the family.

The typography is most pleasing, with important terms or characters in bold-face type. The binding, however, reveals immediate evidence of rather cheap and careless workmanship.

The hope of the senior author that taxonomists will recognize the value of anatomical characters in the delimitation of all taxonomic groups from families down to species seems to be somewhat optimistic, if the extent to which readily available cytomorphological, not to mention embryonomic, data have been ignored in the past by all

save a few systematic botanists is any criterion. In any event, for plant morphologists this is unquestionably the most useful reference work ever compiled.

But anatomy alone will not solve all taxonomic problems in the Angiosperms: the aid afforded by the other morphological fields must also be taken into consideration. When the data of anatomy, of microsporogenesis, and megagametogenesis, plus those of embryonomy and cytology, are all brought together, we may get the answer to the ancient and harrowing question: "What is a species?"

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Pomona, California

**Structure of Molecules and the Chemical Bond.** Y. K. Syrkin and M. E. Dyatkina; translated and revised by M. A. Partridge and D. O. Jordan. New York: Interscience; London: Butterworths Scientific Pubs., 1950. 509 pp. \$8.75.

The first chapter of this book includes an introduction to wave-mechanical ideas and the hydrogen-atom wave functions, and the second develops the periodic table. The next five chapters develop the theory of the chemical bond, taking up in order the covalent bond, saturation and direction of bonds, resonance of valence structures, resonance of covalent and ionic structures, and the molecular-orbital method. Then comes a chapter on diatomic spectra, dealing chiefly with the subject of potential energy curves. The next few chapters take up particular properties: vibrational frequencies and interatomic distances, dipole moments, bond energies, and intermolecular attraction. The three chapters following deal with certain types of compounds: crystals, complexes, and the boron hydrides. The last three chapters are rather more mathematical, dealing with the calculation of resonance energy in aromatic molecules and giving a number of derivations whose results are quoted earlier.

The book deals with the correlation and interpretation of observed structural data, and with the interpretation of chemical behavior in structural terms. Methods of determining molecular structure are not discussed. The mathematical level, except for the final chapters, is not demanding but is adequate; in fact, we feel it strikes just the right pitch, especially in the first and third chapters, which treat basic wave mechanics and Heitler-London theory, respectively.

This task of presenting the quantum theory of chemical bonding without using much mathematics is one of the most difficult that any teacher faces. There are several good books on the subject. Does this book offer anything new and useful? We think it does. First, the presentations of several basic ideas, though not new or flawless, are well done. Second, the book gives a wealth of experimental data, much more than is usual, to illustrate the topics discussed; enough data are given for the reader to see for himself just how well the rules are obeyed.

The way in which these data are given, however, and this wealth of illustration, give rise to our chief criticism. The data are presented uncritically and without adequate

references, and no indication is given of their reliability. Similarly, structural interpretation and speculation on various cases are given uncritically and are, we feel, carried too far; the chapter on the boron hydrides is an example of this. The concepts of modern valence theory are very useful, but their application to chemical problems is an art, and a delicate art at that, rather than a routine logical procedure; one must be able to judge which theoretical conclusions are absolutely sure, and which are speculative. The student should develop this ability to place his bets wisely. We fear that this book will not help him to cultivate this ability as much as it could.

The text seems uneven. We liked the treatment of van der Waals forces but disliked that of the hydrogen bond; we thought the treatment of vibrational frequencies too superficial and empirical, and were surprised to find no discussion of such correlations as Badger's rule; we felt the discussion of metallic structures was far too brief. Some of this unevenness may arise from the revision of the book during translation; but on the whole we feel that the translators are to be commended. Some of the better sections, notably the chapter on molecular orbital theory, are among those that were rewritten.

We can recommend the book as a useful addition to the textbooks on this subject; if the critical viewpoint can be externally supplied, this book should be valuable and stimulating. But we should not advise a student to read it without concurrent discussions with someone learned in the art of which it treats.

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**A History of Experimental Psychology.** 2nd ed. Edwin G. Boring. New York: Appleton-Century-Crofts, 1950. 777 pp. \$6.00.

Boring has revised his history of experimental psychology. Important news for psychology this—the revision of a classic. During the twenty-odd years since the publication of the first edition, nearly every contemporary psychologist has been stimulated by it. In revision, the classic will achieve even greater importance.

The second edition is a true revision. In Professor Boring's own estimate (a fair one), "... the new edition is about one-third larger than the old, is one-half new writing and uses for its other half about two-thirds of the old edition." The treatment of the emergence of science (22 pp.) now throws into relief the problem of the great man versus the *Zeitgeist* in the interpretation of history, and Boring returns again and again to this problem. The emergence of psychology within science, particularly within physiology (127 pp.), is treated without much change from the first edition. The discussion of the emergence of psychology within philosophy (116 pp.) includes a new chapter on the Scottish faculty school and the French materialists, as well as a new section on Kant. The founding of experimental psychology by Fechner, Helmholtz, and Wundt (73 pp.) is little changed. The establishment of modern psychology in Germany (106

pp.) includes a new section on Hering and a revised treatment of Külpe; the establishment of modern psychology in Great Britain (44 pp.) is new in considerable part. The establishment of modern American psychology (79 pp.) gives an old chapter on the pioneers and a new chapter on functionalism at Chicago and Columbia, and within educational psychology and mental testing. The old survey of psychology by decades is gone, being replaced by new chapters on Gestalt psychology (33 pp.), behavioristics (44 pp.), brain function (28 pp.), and dynamic psychology (43 pp.). The book ends with a reassessment of psychology (9 pp.) as Boring now sees it.

Like the old, the new edition treats history in terms of personalities. The life, the development of ideas, the impact on students and colleagues, are described for each of psychology's great men and most of its near-great. Here the lecturer can find assembled those tidbits of personal information that bring the dead past alive for the student. Here are not only the ideas of the past, but also an interpretation of how they came into being, with interesting conclusions about the role of the great man in history.

Knowing that this book is a true revision, which, nevertheless still treats history in terms of personalities, psychologists will ask but one question about it. Does it, now, really go beyond the development of structural psychology; beyond sensation, perception, and the classical treatment of the higher mental processes; beyond that somewhat limited group of men who arrogated to themselves the name of experimental psychologists and, by implication, relegated the student of learning, the mental tester, the social psychologist, and others to fields only partially within the realm of science? There is no simple answer to the question.

Twenty years have made a change in Boring. The great events in psychology's history are now Fechner's *Elemente der Psychophysik*, Ebbinghaus' *Ueber das Gedächtnis*, and Freud's *Die Traumdeutung*. The lives and something of the ideas of such moderns as Holt, Tolman, Hull, Skinner, Sears, Lashley, Lewin, and Murray are described. Psychology's greatest names are Darwin and Freud, Helmholtz and James, and Boring is no longer concerned with whether one can properly call these men "experimental psychologists" or even "psychologists." Titchener is now "important in the history of American psychology" rather than "very important," as the first edition held him to be. Dynamic psychology merits a whole chapter to itself, a chapter which leaves the impression that much of the future belongs to this field. On the other hand, an uncritical reader of the index might conclude that Wundt and McDougall are the only names of importance in the history of social psychology. Thomas Brown's secondary principles of association are incompletely listed in a sentence, whereas Wundt's tridimensional theory occupies a page, and Lotze's theory of space perception covers three and one-half pages. Learning theories, as such, are never developed, even though Ebbinghaus' contribution is now seen to be that of opening up the field of learning rather than the field of higher mental processes.

This reviewer is in doubt as to whether he should criti-

cize Boring for his omissions in broadening the term "experimental psychology" or praise him for broadening it as much as he has. The *Zeitgeist* has worked on Boring, but, as a psychologist might except, it has not completely changed the personality of twenty years ago. Since the book will, and should, influence at least one more generation of psychologists, it can only be concluded that the accidents of personality will produce a generation better oriented in the history of experimental psychology narrowly defined than in the history of experimental psychology broadly defined.

Readers of the first edition will not be surprised to hear that the second edition is written for readers who have more than a passing acquaintance with psychological terms and ideas. For such readers the new book will be superbly clear, far more so than the first edition. At times it will purposely amuse. Frequently it will sparkle with stimulating integrations and contrasts. It will not distract with errors of proof or print. It is a classic, revised and much improved.

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\* The views expressed in this review are those of the author and do not necessarily represent the official views of the United States Air Force.

## Scientific Book Register

- Structural Chemistry of Inorganic Compounds**, Vol. I. Walter Hückel; translated by L. H. Long. New York: Elsevier, 1950. 437 pp. \$9.00.
- Pathologic Physiology: Mechanisms of Disease**. William A. Sodeman, Ed. Philadelphia: Saunders, 1950. 808 pp. \$11.50.
- Coléoptères Curculionides**, Part I: *Faune de France*, Vol. 52. Adolphe Hoffmann. Paris, France: Paul Lechevalier, 1950. 486 pp.
- Coléoptères Psélaphides; Faune de France**, Vol. 53. René Jeannel. Paris, France: Paul Lechevalier, 1950. 421 pp.
- Organic Syntheses**, Vol. 30. Arthur C. Cope, Ed. New York: Wiley; London: Chapman & Hall, 1950. 115 pp. \$2.50.
- The Theory of Valuations**. O. F. G. Schilling. New York: American Mathematical Society, 1950. 253 pp. \$6.00.
- Forest Products**. Nelson Courtlandt Brown. New York: Wiley; London: Chapman & Hall, 1950. 399 pp. \$5.00.
- Existence Theorems in Partial Differential Equations**. Dorothy L. Bernstein. Princeton, N. J.: Princeton Univ. Press, 1950. 228 pp. \$2.50.
- Mathematical Snapshots**. Rev. ed. H. Steinhaus. New York: Oxford Univ. Press, 1950. 266 pp. \$4.50.
- The Friction and Lubrication of Solids**. F. P. Bowden and D. Tabor. New York: Oxford Univ. Press, 1950. 337 pp. \$7.00.

# Association Affairs

The Cleveland Meeting, December 26-30, 1950

## II—The Programs in Mathematics, Physics, Astronomy, and Chemistry

LAST week we described briefly some of the high lights of the **Annual Science Exposition**, which is so important a part of the Annual Meetings of the AAAS. This week we offer a preview of the scientific programs to be presented at Cleveland.

### PROGRAM OF SECTION A—MATHEMATICS

**Sessions 1-6.** Section A will cosponsor with The Biometric Society, Eastern North American Region, the following six-session symposium on *Mathematical Biology and Biometry*:

**Part I.** Wednesday morning, December 27, Nicolas Rashevsky, Committee on Mathematical Biology, University of Chicago, presiding.

1. "The Kinetics of Reactions in Biological Systems." Herman Branson, Department of Physics, Howard University.

2. "On Some Thermodynamic Aspects of Stationary Systems." J. Z. Hearon, Department of Physiology, University of Chicago.

**Part II.** Wednesday afternoon, December 27, Leslie Nims, Biology Department, Brookhaven National Laboratory, presiding.

1. "Geometry, Statistics, Biophysics." Karl Menger, Department of Mathematics, Illinois Institute of Technology, Chicago.

2. "Applications of Random Net Theory to the Mathematical Biology of the Nervous System and to Epidemiology." Anatol Rapoport and Alfonso Shimbelt, Committee on Mathematical Biology, University of Chicago.

3. "The Application of Latent Structure Analysis to Some Social Science Problems." Paul F. Lazarsfeld, Department of Sociology, Columbia University.

**Part III.** Thursday morning, December 28, Karl Menger presiding.

1. "Mathematical Biology of Social Phenomena." Nicolas Rashevsky.

2. "On Dominance Relations and the Structure of Animal Societies." H. G. Landau, Committee on Mathematical Biology, University of Chicago.

**Part IV.** Thursday afternoon, December 28, Herman Branson presiding.

1. "A Physical Theory of Decompression Sickness." Leslie Nims.

2. "Near Balance Rectangular Lattices." Boyd Harshbarger, Statistical Laboratory, Virginia Polytechnic Institute, Blacksburg.

**Part V.** Friday morning, December 29, Anatol Rapoport presiding.

1. "Theoretical and Experimental Aspects in the Removal of Airborne Matter by the Human Respiratory

Tract." H. D. Landahl, Committee on Mathematical Biology, University of Chicago.

2. "Two Opposite Aspects of the Dose-Frequency Curve in Radiobiology." I. Opatowski, Committee on Mathematical Biology, University of Chicago.

**Part VI.** Friday afternoon, December 29, Boyd Harshbarger presiding.

1. "A Formula for the Velocity of Conduction of Excitation." I. Opatowski.

2. "The Interpretation of Lethality Statistics in Terms of a Continuous Stochastic Process." George Sacher, Division of Biological and Medical Research, Argonne National Laboratory.

**Sessions 7-8.** Section A has arranged a two-session symposium on *Mathematics in Applied Science*.

**Part I.** Saturday morning, December 30, Robert F. Rinehart, Department of Mathematics, Case Institute of Technology, presiding.

1. "Operations Research and Mathematicians." Philip M. Morse, Department of Physics, Massachusetts Institute of Technology.

2. "Finite Difference Methods in the Theory of Structures." Oscar Hoffman, Department of Civil Engineering, Case Institute of Technology.

3. "Deformations and Stresses in Bourdon Tubes." Robert A. Clark, Department of Mathematics, Case Institute of Technology.

4. "Numerical Solution for Nonlinear Elliptic Partial Differential Equations." L. R. Turner, Lewis Flight Propulsion Laboratory, Cleveland.

**Part II.** Saturday afternoon, December 30, Sidney W. McCuskey, Department of Mathematics, Case Institute of Technology, presiding.

5. "Nonequilibrium Mathematics in Engineering." Brockway McMillan, Bell Telephone Laboratories.

6. "On the Use of Mappings in Designing Cascades for Compressible Flows." George R. Costello, Lewis Flight Propulsion Laboratory, Cleveland.

7. "Theory of Geodesics Applied to Electromagnetic Propagation between Curved Plates." Kaiser Kunz, Department of Electrical Engineering, Case Institute of Technology.

### PROGRAM OF SECTION B—PHYSICS

**Session 1.** Wednesday morning, December 27, symposium on *Fifty Years of Quantum Theory*, Robert B. Brode, Department of Physics, University of California at Berkeley, presiding.

1. "Fifty Years of Quantum Theory." Karl K. Darrow, Bell Telephone Laboratories.

2. "Developments from Wave Mechanics." Edward U. Condon, National Bureau of Standards.



**Session 2.** Wednesday afternoon, December 27, joint symposium of Section B and Section D—Astronomy on *Fifty Years of Quantum Theory in Astronomy*, Alfred H. Joy, Mount Wilson Observatory, presiding.

1. "Atomic Spectra for Astrophysics." Charlotte Moore Sitterly, National Bureau of Standards.

2. "Interpreting Spectra of Stellar Atmospheres in Gaseous Nebulae." Lyman Spitzer, Jr., Princeton University Observatory.

3. "Energy Sources in the Stars and their Influence on Stellar Structure." Geoffrey Keller, Perkins Observatory, Delaware, Ohio.

**Session 3.** Thursday morning, December 28, joint symposium of Section B and Section E—Geology and Geography on *The Implications of Nuclear Phenomena in Geology*, Edward Teller, Institute of Nuclear Studies, University of Chicago, presiding.

1. "Origin of the Universe and the Earth." Harrison Brown, Institute of Nuclear Studies, University of Chicago.

2. "Geologic Processes in the History of the Earth." Patrick M. Hurley, Massachusetts Institute of Technology.

3. "Existing Distributions of Materials on the Earth." George Bain, Amherst College.

**Session 4.** Thursday afternoon, December 28 (will be reported next week).

#### AMERICAN METEOROLOGICAL SOCIETY

Wednesday afternoon, December 27, Conference of  
Midwestern Meteorologists.

#### OAK RIDGE INSTITUTE OF NUCLEAR STUDIES JOINT PROGRAM WITH THE OAK RIDGE NATIONAL LABORATORY

**Session 1.** Thursday morning, December 28, William G. Pollard, Oak Ridge Institute of Nuclear Studies, presiding.

1. "The Stockpiling and Rationing of Scientific Manpower." H. D. Smyth, U. S. Atomic Energy Commission, Washington, D. C.

2. "Impact of the Developments in Atomic Energy on the Sciences." E. P. Wigner, Princeton University and Oak Ridge National Laboratory.

3. "The Role of Chemistry in the Development of Atomic Energy." J. A. Swartout, Oak Ridge National Laboratory.

**Session 2.** Thursday afternoon, December 28, seminar on *Ten Years of Atomic Energy—A Review of Progress*. Alvin M. Weinberg, Oak Ridge National Laboratory, presiding.

*Members of the Seminar Panel:* M. C. Leverett, NEPA Project, Fairchild Engine and Airplane Corporation; Philip Sporn, American Gas & Electric Service Corporation; C. G. Suits, General Electric Company; J. A. Swartout, Oak Ridge National Laboratory; E. P. Wigner; and W. H. Zinn, Argonne National Laboratory.

Among the specific topics to be discussed in this seminar will be the outlook for the development of atomic power (led by Zinn); the role of military developments

of atomic power (led by Leverett); and the question of how private industry can best participate in the development of atomic energy (led by Sporn and Suits).

#### PROGRAM OF SECTION D—ASTRONOMY

**Session 1.** Tuesday morning, December 26, contributed papers (to be announced), J. J. Nassau, Warner and Swasey Observatory, Case Institute of Technology, presiding.

**Session 2.** Tuesday afternoon, December 26, contributed papers (to be announced), Alfred H. Joy presiding.

**Session 3.** Tuesday evening, December 26, address of the retiring vice president of Section D. "Stellar Explorations with the Spectrograph." Alfred H. Joy.

**Session 4.** Wednesday morning, December 27. Inspection of the equipment of the Warner and Swasey Observatory, and possible session for papers.

**Session 5.** Wednesday afternoon, December 27, symposium on *Fifty Years of the Quantum Theory in Astronomy*; joint session of Section B—Physics and Section D—(See program of Section B.)

#### PROGRAM OF SECTION C—CHEMISTRY

The programs of Section C are given only in part; programs in chemistry concerned mainly with biology and medicine will appear next week.

**Tours:** Tuesday, December 26, will be devoted entirely to tours of industrial and academic laboratories. Of the 26 tours planned, the following will be of particular interest to chemists and physicists:

Aluminum Company of America

American Gas Association Laboratory

Case Institute of Technology

Ferro Enamel Corporation

The Glidden Company

B. F. Goodrich Company

Harshaw Chemical Company

Lewis Flight Propulsion Laboratory, NACA

Nela Park, General Electric Company

Republic Steel Company

Sherwin Williams Company

Standard Oil Company (of Ohio)

Thompson Products Auto Album and Aviation Museum

Western Reserve University

**Sessions 1-2.** Symposium on *Advances in Inorganic Chemistry*.

**Part I.** Friday morning, December 29, W. Conard Fernelius, Pennsylvania State College, presiding.

1. Introductory Remarks. W. C. Fernelius.

2. "The Newer Refractories." L. S. Foster, Ordnance Department, Watertown Arsenal.

3. "The Metallurgy of the Less Familiar Elements." B. W. Gonsor, Battelle Memorial Institute.

4. "The Chemistry of Hafnium and Zirconium." E. M. Larsen, University of Wisconsin.

5. "Recent Developments in the Field of the Rare Earths." L. L. Quill, Michigan State College.

*Part II.* Friday afternoon, December 29, W. C. Fernelius presiding.

1. "The Use of Magnetic Susceptibility Measurements in Inorganic Chemistry." P. W. Selwood, Northwestern University.

2. "The Importance of Trace Elements in Chemistry." Roland Ward, University of Connecticut.

3. "The Fundamental Chemistry of Glass." W. A. Weyl, Pennsylvania State College.

4. "Recent Developments in the Field of Coordination Compounds." W. C. Fernelius and B. E. Douglas, Pennsylvania State College.

*Sessions 3-4. Symposium on Forensic Science.*

*Part I.* Saturday morning, December 30, Ralph F. Turner presiding.

1. Introductory Remarks. Ralph F. Turner.

2. "Pathology." Alan Moritz, Western Reserve University.

3. "Pathology." Frank Dutra, University of Cincinnati, School of Medicine.

4. "Pathology." Sam Levinson, University of Illinois, College of Medicine.

5. "Chemistry and Spectroscopy." Charles Umberger, Office of the Chief Medical Examiner, Division of Laboratories, Bellevue Hospital, New York.

*Part II.* Saturday afternoon, December 30, Ralph F. Turner presiding.

1. "The Petrographic Aspects of Scientific Crime Detection." R. H. Jevons, Special Agent, Federal Bureau of Investigation.

2. "Ballistics." J. H. Mathews, University of Wisconsin.

3. "Toxicology." C. W. Muehlberger, State Crime Detection Laboratory, Michigan State Department of Health.

On Saturday noon, December 30, there will be a *Luncheon for all Chemists*, Edward F. Degering, Miner Laboratories, presiding. Roger Adams, Department of Chemistry, University of Illinois, and President of the AAAS, will be guest speaker.

Additional programs that will appeal to those in the

fields of mathematics, physics, astronomy, and inorganic chemistry are concerned with nuclear engineering and atomic power (Section M—Engineering); a four-session symposium on radiobiology (Section Nm—Medicine); and the annual addresses of the Scientific Research Society of America and the Society of the Sigma Xi. An outline of these and other programs will appear in subsequent issues of *SCIENCE*.

RAYMOND L. TAYLOR

*Assistant Administrative Secretary*

#### Life Members

The AAAS Membership Office, 1515 Massachusetts Ave., N.W., Washington 5, D. C., would appreciate receiving information concerning the whereabouts of the following life members. The year indicates when AAAS membership was first obtained, and the address is the last known.

Hugo Blumenthal (1916)

The Sherry Netherlands, 59th St. & 5th Ave., New York City 22

Dr. E. M. Burwash (1922)

20 Wood St., Toronto, Ontario, Canada

A.W. Elliott (1938)

Apartment 2-D, 562 W. 113th St., New York City 25

Miss Mary L. Jackson (1919)

6842 Penn Ave., Pittsburgh, Pa.

Frederick Atkins Johnston (1908)

153 St. Marks Place, New Brighton, Staten Island, N. Y.

Dr. Kwong Yung Kwang (1912)

Lincheng Mines, Lincheng, Chihli Province, Kinkhan Railway via Peking, N. China

Fred I. Lackenbach (1925)

908 Butler Bldg., San Francisco 9, Calif.

Rev. J. D. Marmor

12 E. 115th St., New York City

Dr. Shigeo Yamanouchi (1906)

Department of Botany, University of Chicago, Chicago, Ill.



# News and Notes

## The International Congress of Mathematicians

C. Raymond Adams

Department of Mathematics, Brown University, Providence, Rhode Island

The congress was held at Cambridge, Massachusetts, August 30–September 6 under the auspices of the American Mathematical Society, with Harvard University as host institution and with the American Academy of Arts and Sciences, Boston College, Boston University, Massachusetts Institute of Technology, and Tufts College as co-hosts.

The sessions were formerly opened by Garrett Birkhoff, of Harvard, as chairman of the Organizing Committee, who introduced the president of the congress, Oswald Veblen, of the Institute for Advanced Study in Princeton. Jacques Hadamard, of the Collège de France, was honorary president. In his address of welcome, Veblen observed that by the time of the Oslo Congress in 1936 "the colonial period of American mathematics had ended," and an invitation to hold the next congress in the United States in 1940 was extended and accepted. He paid graceful tribute to his lifelong friend, the late George David Birkhoff, of Harvard, who was to have been president of the congress in 1940 had its postponement not been made necessary by World War II.

In recognition of recent research accomplishments of outstanding merit, the Fields gold medals, each accompanied by an honorarium of \$1,500, were awarded to the Norwegian mathematician Atle Selberg, aged 33, now a permanent member of the Institute for Advanced Study, and to Laurent Schwartz, aged 35, of the University of Nancy, France. The awards were made by Harald Bohr, of the University of Copenhagen, acting as chairman of the International Committee of Selection. He referred to the decision of the committee to limit its choice to young men of already high attainment and great promise, in the face of the numerous and significant contributions made since 1936 by many older mathematicians of established reputation.

Bohr reviewed briefly the work for which the Fields awards were made. In 1896 an estimate was established for the frequency with which prime numbers appear in the succession of positive integers; this is known as the *prime number theorem*. The first and several later proofs of this theorem were based on sophisticated considerations involving the complex zeros of the Riemann zeta-function, and such an eminent expert in the field of number theory as the late G. H. Hardy, of the University of Cambridge, expressed the belief that no "elementary" proof of the theorem could be devised. Selberg has found several such elementary proofs and has substantially increased our knowledge of the distribution of primes among the integers.

In contrast with Selberg, who has introduced new

methods into the study of old problems now regarded as classical, Schwartz has brought forward new fundamental ideas, in particular a fruitful extension of the common notion of function which he terms a *distribution*. He has already made several applications of this idea, which not only makes possible the more elegant formulation of known results of harmonic analysis, but promises to provide a useful tool for attacking many problems in potential theory, spectral theory, and the theory of partial differential equations. The 1948 paper by Schwartz on the theory of distributions "will stand as one of the classical papers of all time," predicted Bohr.

By invitation of the Organizing Committee addresses were given by 22 speakers: A. A. Albert, A. Beurling, S. Bochner, H. Cartan, S. S. Chern, H. Davenport, K. Gödel, W. V. D. Hodge, H. Hopf, W. Hurewicz, S. Kakutani, M. Morse, J. von Neumann, J. F. Ritt, A. Rome, L. Schwartz, A. Wald, A. Weil, H. Whitney, N. Wiener, R. L. Wilder, and O. Zariwki. Conferences on algebra, analysis, applied mathematics, and topology, with about 90 participants, were a feature of the program. At additional sessions more than 400 papers were contributed on algebra and theory of numbers, analysis, geometry and topology, probability and statistics, actuarial science, economics, mathematical physics and applied mathematics, logic and philosophy, and history and education.

At the plenary session on September 6 Marshall Stone, of the University of Chicago, reported plans for the organization of an International Mathematical Union, which had been made by representatives from 22 countries who met August 27–29 in New York City. This union will come into effective existence as soon as the organized mathematicians of 10 countries become adherents under the bylaws formulated by the New York convention. On behalf of his colleagues in Holland, J. G. van der Corput, of the University of Amsterdam, presented an invitation to hold the next congress at Amsterdam in 1954. This invitation was unanimously accepted.

Attendance at the congress—by far the largest gathering of mathematicians ever held—exceeded 2,300 persons, including about 300 representatives and delegates from more than 40 foreign countries, representatives from the U. S., and delegates from 15 American societies and academies. The USSR Academy of Science sent a cable to J. R. Kline, of the University of Pennsylvania, secretary of the congress, expressing appreciation of its invitation and the hope that the congress would be a significant event in mathematical science, but regretting that "Soviet mathematicians, being very much occupied with their regular work, will be unable to attend."

Social events included receptions at the Fogg Museum of Art and the Gardner Museum, a reception and organ recital at Boston University, a tea at Wellesley College, a banquet tendered by Harvard University, and concerts by the Busch Quartet, Richard Dyer-Bennett, and Helen Traubel.

The Econometric Society held its summer meeting at Harvard in conjunction with the congress. Special conferences and symposia were held immediately preceding or directly after the congress on fluid mechanics, on the theory of functions of several complex variables, and on algebraic geometry at Harvard; on differential geometry at Boston University; on computing machinery at the National Bureau of Standards, Washington, D. C.; on differential equations at the University of Maryland; and on plasticity at Brown University.

In his address Veblen remarked, "Mathematicians are terribly individual." So, also, is mathematics, in the sense that it has become specialized to an extent that makes out of place here a more detailed description of the scientific program of the congress. For such a re-

port interested readers must await the publication of the *Proceedings* of the congress.

The sessions gave ample evidence that on a wide front the boundaries of mathematical knowledge are being pushed back, as rapidly as they have ever been in the past, by a host of competent workers and by a substantial number of men of exceptional imagination and power. The increasing mathematical requirements of government and industry, both in the U. S. and other countries, and the availability of modern calculating machines, are accelerating the influx of problems from the natural sciences that not only has long been recognized as healthful and vitalizing, but also as actually essential to the well-rounded development of mathematics. Whether the present generation of mathematicians includes men of the stature of Gauss (1777-1855), Riemann (1826-66), Poincaré (1854-1912), and Hilbert (1862-1943) can only be determined later. But we can be confident that this generation will prove to be responsible trustees of the tradition of scientific progress that has been handed down by its predecessors.

## American Chemical Society's 118th National Meeting

Walter J. Murphy  
*American Chemical Society*

An appeal to President Truman to act at once to prevent a dangerous waste of scientific manpower in the current international crisis was made by the American Chemical Society, through its Board of Directors, at the society's 118th national meeting, which was held in Chicago September 3-8.

In a unanimously adopted resolution, the board specifically asked the President to designate some one Federal agency to formulate and administer an effective program for the training and use of technical personnel in time of national emergency. The resolution also invited other scientific associations to join the ACS in setting up a national committee to work with the government on this problem.

Ernest H. Volwiler, in his presidential address, urged Congress to spell out in selective service legislation a three-point policy on the drafting of scientists and their utilization in the armed forces. His three points were: that key scientists in industry, government, and education be left in their posts to carry through total mobilization of the nation; that scientists in the armed forces be assigned to the tasks in which their special training would be most valuable; and that outstanding science students be deferred while they completed their training. No blanket deferment for chemists, chemical engineers, or other scientists is sought by the ACS, it was emphasized; the society merely seeks the most efficient utilization of the special skills of all scientists and engineers.

A serious lag in scientific research in colleges was reported by Charles A. Kraus, professor emeritus in Brown University, who received the society's Priestley Medal at

a general assembly in the Hotel Stevens, convention headquarters. Dr. Kraus, a director and former president of the ACS, said the failure of many colleges to sponsor adequate research programs resulted to a large extent from lack of appreciation of the importance of research and not from financial limitations alone. Yet, he said, "our continued well-being, indeed our very existence," may depend on the effective application of research to our ever-growing problems.

The names of eight 1951 award winners were announced by Dr. Volwiler. They are: Garvan Medal—Katherine B. Blodgett, General Electric Company Research Laboratory, Schenectady, N. Y.; American Chemical Society Award in Pure Chemistry—John C. Sheehan, Massachusetts Institute of Technology; Fritzsche Award in Essential Oils—Edgar Lederer, Institut de Biologie Physico-Chimique, Paris, France; Precision Scientific Company Award in Petroleum Chemistry—Louis Schmerling, Universal Oil Products Company, Chicago; Fisher Award in Analytical Chemistry—Robert H. Willard, University of Michigan; Borden Award in the Chemistry of Milk—Thomas L. McMeekin, Eastern Regional Research Laboratory, Philadelphia; Paul-Lewis Laboratories Award in Enzyme Chemistry—Arthur Kornberg, National Institutes of Health, Bethesda, Md.; Eli Lilly & Company Award in Biological Chemistry—John M. Buchanan, University of Pennsylvania School of Medicine.

A new theory of virus invasion of living cells, which may hold far-reaching implications for the prevention and treatment of virus diseases, was announced in one of the 1,181 technical papers—an all-time record—presented at the meeting. Based on the discovery that a virus at-

tack on a specific cell is a two-step process, the theory explains that in the first step the virus becomes attached to the target cell as the result of a purely electrical attraction, governed by metallic ions normally present in the cell's environment, according to Theodore T. Puck, head of the Department of Biophysics in the University of Colorado Medical Center. Laboratory experiments have shown that by introducing certain other metallic ions, such as zinc, which are not ordinarily present, it is possible to block this attraction and thus make the cell immune to the virus, Dr. Puck said.

Evidence that arteriosclerosis may be prevented through the use of the vitaminlike substance inositol was reported by Stephanie J. Ilka, William C. Felch, and Louis B. Dotti, of St. Luke's Hospital, New York. Their experiments on animals indicate that inositol can effectively reduce the blood's content of cholesterol, the fatty compound widely suspected of causing arteriosclerosis by clinging to the arterial walls.

Broad new fields of application for antibiotics may be opened by discoveries concerning the special properties of two compounds announced at the meeting. One of the new compounds, known as Netropsin, "has been found to be active against clothes moth larvae and the black carpet beetle," according to A. C. Finlay and three colleagues, of Charles Pfizer & Company, Brooklyn. The other new antibiotic, which was isolated from the roots of a tropical flowering plant instead of from the soil, has shown high potency as a fungicide. This substance, called Plumericin from the name of the source—*Plumeria multiflora*—was reported by John Little, head of the De-

partment of Agricultural Biochemistry at the Vermont Agricultural Experiment Station, who is testing more than 1,700 plants in a search for other antibiotics.

Successful preparation of both curium metal and americium metal was announced at a session on the chemistry of the actinide elements. Curium metal is so radioactive that it glows as brightly as a flashlight in the dark, according to J. C. Wallman, W. W. Crane, and B. B. Cunningham, of the University of California. With berkelium (element 97) and californium (element 98), discovered in the past year, nuclear chemists now believe the actinide series runs as high as 103, although they are not sure the last few elements in the series ever will be isolated, said Glenn T. Seaborg, University of California.

Effective methods of disposing of radioactive waste materials, new insecticides and other agricultural chemicals from petroleum, and recent progress in the production and use of cortisone and ACTH also were reported at the meeting, in which 8,000 chemists and chemical engineers participated.

Appointment of John H. Nair, assistant director of research of Thomas J. Lipton, Inc., Hoboken, N. J., as chairman of the society's Diamond Jubilee Committee was announced by Dr. Volwiler at close of the meeting. Dr. Volwiler said the society's anniversary celebration in New York in September, 1951, and the sessions of the International Union of Pure and Applied Chemistry and the International Congress of Pure and Applied Chemistry, scheduled for the same month, will be held as planned unless they are precluded by the international situation at that time.

## About People

**Felix T. Adler**, member of the Institute for Advanced Study, Princeton, 1941-42, and **Julius Ashkin**, formerly assistant professor at the University of Rochester, have been appointed to the faculty of the Carnegie Institute of Technology Physics Department.

Now a member of the Department of Physiology and Pharmacology, Wayne University, **Marion I. Barnhart** will continue at Wayne her research work in cellular physiology. Miss Barnhart has just completed her work for the doctor's degree at the University of Missouri.

**Ralph Buchsbaum**, formerly research associate in the Department of Zoology and in the Institute of Radiobiology and Biophysics at the University of Chicago, has been appointed professor of zoology in the Department of Biological Sciences, University of Pittsburgh. He will

be in charge of invertebrate studies and will continue his investigations in cell biology.

**Nicholas D. Cheronis**, formerly at the Wright Branch of Chicago City College, has been appointed professor and chairman of the Department of Chemistry of Brooklyn College.

Appointed managing editor of the *Biological Bulletin*, to succeed H. Burr Steinbach, is **Donald F. Costello**, of the University of North Carolina.

The inauguration of **Earl Hampton McClenney, Sr.**, as third president of St. Paul's Polytechnic Institute, Lawrenceville, Va., took place October 12. Among the delegates attending were Reuben Roosevelt McDaniel, American Mathematical Society; Lorin A. Thompson, American Academy of Political and Social Science; Keturah E. Whitehurst, American Psychological Association; M. E. V. Hunter, Ameri-

can Home Economics Association; and John Peter Wynne, National Philosophy of Education Society.

A Special Fellow of the National Cancer Institute, U. S. Public Health Service, for the coming year is **Alfred Novak**, of the Department of Biological Science, Michigan State College. He will work with **Henry Borsook** on the biosynthesis of proteins at California Institute of Technology.

**Jane M. Oppenheimer**, associate professor of biology at Bryn Mawr College, has been awarded a Rockefeller fellowship for the academic year 1950-51, to enable her to make an international survey of the problem of raising the general level of scientific understanding in the world today.

## Visitors

Under the sponsorship of ECA, **Demetrius Thalellis**, director of the Plant Improvement Institute, Salon-



ika, and **Demetrius S. Katakouninos**, director of the Soils Laboratory, Athens, Greece, have been making a study of saline and alkaline soils and their relation to plant growth, on the Davis campus of the University of California. **Erik Hjalmer Akerberg**, associate professor of research and technical instruction, Royal Agricultural College of Sweden, also visited the Davis campus, to study forage crop improvement.

The Institute for Fluid Dynamics and Applied Mathematics, University of Maryland, recently presented **Werner Heisenberg** in two public lectures. Dr. Heisenberg is director of the Max Planck Institute for Physics, University of Göttingen, Germany. He spoke on the "Statistical Theory of Turbulence" and the "Present Situation in the Theory of Elementary Particles."

**Nobuyoshi Kato**, Kyoto University, **Yoshihiro Asami**, Hokkaido University, and **Yasushi Watanabe**, Tohoku University, Japanese educators, are making a tour of engineering colleges in the U. S. under the Exchange-of-Persons Program sponsored by the Department of the Army's Far East Command. The program was arranged by the Institute of International Education.

**Charity Weymouth**, director of the Tissue Culture Section of the Chester Beatty Research Institute, Royal Cancer Hospital, London, is visiting the Tissue Culture Laboratory of the University of Texas Medical Branch, Galveston, for special work with **Charles M. Pomerat**. She will also visit other representative tissue culture laboratories in this country.

## Fellowships

The Institute of Industrial Health of the University of Cincinnati is accepting applications for a limited number of fellowships for graduate studies leading to the degree of Doctor of Industrial Medicine. Any registered physician who is a graduate of a Class A medical school and who has completed satisfactorily two years of residency (including internship) in a hospital

accredited by the American Medical Association may apply. The course of instruction consists of a two-year period of intense preliminary training in the basic phases of industrial medicine, followed by one year of practical experience under adequate supervision in industry. During the first two years, the stipends vary from \$2,100 to \$3,000. In the third year, the candidate will be compensated for his service by the industry in which he is completing his training. Requests for additional information should be addressed to the Institute of Industrial Medicine, College of Medicine, Cincinnati 19, Ohio.

The World Health Organization is offering 9 to 12 fellowships for foreign study in the field of health, available for 1951. Grants are for periods of two to three months for observation and up to 12 months for study. Transportation is provided to the place of study and in the country visited. The stipend is from \$160 to \$200 a month for those studying in one place, and from \$240 to \$300 for those moving about. Applications may be obtained from the Educational Programs Branch, Division of International Health, U. S. Public Health Service, Washington, D. C., and must be returned in triplicate by January 1, 1951.

The 11th annual **William Lowell Mathematical Competition** will be held March 31, 1951, under the sponsorship of the Mathematical Association of America. The competition is open to undergraduate students in universities and colleges of the U. S. and Canada. The questions will be taken from the fields of calculus (elementary and advanced), with applications to geometry and mechanics not involving techniques beyond the usual applications, higher algebra (determinants and theory of equations), elementary differential equations, and geometry (advanced plane and solid analytic). Prizes to be awarded to the departments of mathematics of the institutions with the winning teams are \$400, \$300, \$200, and \$100. In addition, prizes of \$40, \$30, \$20, and \$10 will be awarded to the members of these

teams, \$50 to each of the five highest contestants, and \$20 to each of the succeeding five highest contestants. Each winner will receive a medal. A \$1,500 **William Lowell Putnam Prize Scholarship** at Harvard University or at Radcliffe College will go to one of the first five, to be available immediately or on completion of the student's undergraduate work. Any college or university wishing to enter contestants may secure application blanks from L. E. Bush, 112 Albertus Magnus Hall, College of St. Thomas, St. Paul 1, Minn. Applications must be filed not later than March 1, 1951.

## Colleges and Universities

An interscience commission has been established at the **University of Pennsylvania** in recognition of the growing need for closer interaction between workers in the physical sciences and engineering, and those in the biological and medical sciences. Functions of the commission include integration of those research programs which bring the influence of the physical sciences into the solution of medical or biological problems, and the survey of physical facilities required for this type of interscience. Only students of high caliber, willing to devote four years of full-time study to doctoral programs, are encouraged to elect the new area of specialized study. The chairman of the commission is **Britton Chance**, director of the Johnson Foundation for Medical Physics. **David R. Goddard**, professor of botany, and **S. Reid Warren**, professor of electrical engineering in the Moore School of Electrical Engineering, are members of the Advisory Committee.

The **Einar Naumann Medal**, one of the highest honors given for work in limnology, has been awarded to the **University of Wisconsin** by the International Association of Limnology, at its annual meeting in Ghent, Belgium, in memory of two pioneers in the field, the late President Emeritus **Edward A. Birge** and the late **Chauncey Juday**. Professor Birge, who died June 9, 1950, at the age of 98, was the oldest holder of the Ph.D. degree in

the U. S., the oldest member of Phi Beta Kappa, and the oldest active member of a university faculty. Birge and Juday began their work together in 1905, and their association lasted until Juday's death in 1944. The medal is named in honor of a Danish limnologist who was a contemporary of Birge and Juday.

Recent appointments to the **Applied Physics Laboratory, The Johns Hopkins University**, are Charles I. Beard, formerly with the Magnolia Petroleum Co., Dallas, Texas; Robert W. Hart, of Catholic University; Fred K. Elder, Jr., of the University of Wyoming; John B. Garrison, from the University of Chicago; John J. Sopka, Tufts College; Joseph H. Zelinaki, Pennsylvania State College; Jordan J. Markham, Brown University; Gwynne B. Swartz, University of Maryland; Robert P. Rich, The Johns Hopkins University; Raydeen R. Howard, Duke University; and William Liben, Brookhaven National Laboratory.

Norman O. Smith, formerly of the Chemistry Department of the University of Manitoba, has joined the faculty of **Fordham University** as associate professor of physical chemistry. M. J. McGuinness, Jr., formerly research chemist for E. I. du Pont de Nemours and Company, has joined the faculty as assistant professor of chemistry.

## Industrial Laboratories

**Eli Lilly and Company** has appointed A. Lee Caldwell head of its newly created Product Technical Service Department. Dr. Caldwell was formerly head of the company's nutrition and vitamin research.

**Antara Products, General Aniline & Film Corporation**, 444 Madison Ave., New York 22, has available on request *Data Bulletin #303*, an 8-page folder giving properties, characteristics, uses, and handling information for 1,4-butanediol.

**Nutritional Biochemicals Corporation** has issued a new catalogue listing nearly 500 biochemicals of nutritional, biological, microbiological, and medical significance. In-

cluded are amino acids, nucleoproteins, purines, pyrimidines, crystalline vitamins, accessory growth factors, miscellaneous biochemicals, media for microbiological procedures, purified proteins, carbohydrates, and various experimental diets. Copies can be obtained by writing to Nutritional Biochemicals Corporation, Cleveland 5, Ohio.

An injectable form of terramycin has been made available to the medical profession by **Chas. Pfizer & Co., Inc.**, sole producer of the new drug. Terramycin Intravenous, the name under which this new dosage form will be marketed, will be especially valuable for treatment where immediate therapeutic action is essential and in the treatment of hospitalized patients who cannot take the customary forms of oral antibiotic medication.

**The Gulf Oil Corporation** will assist in the establishment of a chair of geology at the American University of Beirut, Lebanon, beginning this academic year. Roy A. Wilson, a geologist with Gulf, will hold the chair and will teach physical geography, engineering geology, and physical geology, all new subjects in the university.

## Meetings and Elections

**The American Petroleum Institute** will hold its 30th annual meeting in Los Angeles, November 13-16, at the Biltmore and Ambassador Hotels. In addition to almost 100 committee sessions, which will begin November 9, two general and numerous group sessions will be held. Frank M. Porter, president of the institute, will address the general session on November 15, and Benjamin F. Fairless, president of United States Steel Corporation, and Reese H. Taylor, president of Union Oil Company of California, will be speakers on November 16. Further information and the advance program may be obtained from the Department of Information, American Petroleum Institute, 50 W. 50th St., New York 20.

Governor Ernest Gruening will address the **Alaskan Science Conference**, to be held in Washington un-

der the sponsorship of the National Academy of Sciences-National Research Council, November 9-11. The conference will consist of 20 individual sessions, including 3 symposia and one public meeting at which government officials will speak and special Alaskan films will be shown. The organization of the conference has been carried out by a steering committee appointed by the chairman of the National Research Council, and includes representatives from the Departments of the Interior, Agriculture, Commerce, Army, Navy, Air Force, the Federal Security Administration, the Arctic Institute of North America, the Smithsonian Institution, the American Geographical Society, the University of Alaska, and the Alaskan Territorial Government.

**The Medical Women's International Association's** 6th congress was held September 10-16 at the Woman's Medical College, Philadelphia. The opening exercises of the 101st year of the Woman's Medical College, at which A. Charlotte Ruys, of Amsterdam, president of the congress spoke, were a feature of the meeting. A program of clinic demonstrations and scientific papers by the faculty of the college, under the chairmanship of L. Kracer Ferguson, professor of surgery, was also included. New officers elected at the association's meeting are Ada Chree Reid, New York City, president; G. Montreuil-Strauss, France, Inger Haldorsen, Norway, Zaida Eriksson-Lihr, Finland, Grace Cuthbert, Australia, Doris Odum, England, and M. T. Cassassa, Italy, vice presidents. Dr. Odier-Dollfus, France, is honorary treasurer, and Janet Aitken, England, honorary secretary. Their terms of office will run until the next international congress, to be held in four years, if world conditions permit.

Two papers, one on the effect of the sun's altitude on daylight, by R. H. Bingham and Herman Hoerlin, research scientists at Anasco Research Laboratories, Binghamton, N. Y., and the other a short-cut photo process that eliminates fixing and washing of prints, by E. C. Yackel,

Kodak Research Laboratories, were high lights of the convention of the **Photographic Society of America** in Baltimore October 18-21. The organization elected 8 men to honorary membership and cited 23 new fellows and 69 associates. New officers of the PSA Technical Division, which represents the national society in matters of standards of photographic materials, equipment, and processes, are William F. Swann, Eastman Kodak Company, Rochester, chairman; Theron T. Holden, Graflex, Inc., Rochester, vice chairman; and William H. Fritz, National Carbon Division, Union Carbide and Carbon Corp., secretary-treasurer.

Three hundred chemists and chemical engineers attending a combined meeting of Oklahoma's three local sections of the **American Chemical Society** at Bartlesville heard Wayne E. White, research chemist for the Ozark-Mahoning Company, Tulsa, state that treatment of all drinking water with fluorine compounds to improve the dental health of the nation is now virtually assured.

**The Association of Consulting Chemists and Chemical Engineers** elected the following officers at its annual meeting, October 24: president, Erwin Di Cyan, Di Cyan & Brown; vice president, Earl D. Stewart, Schwarz Laboratories; treasurer, Robert S. Aries, Robert S. Aries & Associates; and secretary, Albert Parsons Sachs, consulting chemical engineer, New York City.

## NRC News

The American Cancer Society will inaugurate in 1951 a program to help newly trained scientists establish themselves in the field of cancer research. The **Grants for Scholars in Cancer Research**, as the program will be known, are designed to bridge the gap between completion of fellowship training and the period when the scientist has thoroughly demonstrated his competence as an independent investigator. A limited number of American Cancer Society scholars will be appointed annually on recommendation of the

Committee on Growth of the National Research Council. A grant of \$18,000, payable over three years, will be made directly to each scholar's institution by the society as a contribution toward his support and research. Medical schools, hospitals, research institutes, and other institutions with a substantial interest in cancer research are invited to submit applications for these grants. They should be submitted before *January 1, 1951*, for grants to be effective July 1. Inquiries and requests for forms should be addressed to the Executive Secretary, Committee on Growth, National Research Council, 2101 Constitution Ave., Washington 25, D. C.

The Medical Fellowship Board of the NRC is now accepting applications for postdoctoral research fellowships for 1951-52 under the following programs: **National Research Fellowships in the Medical Sciences**, supported by grants from The Rockefeller Foundation, provide opportunity for training in research in all branches of medical science. They are open to citizens of the U. S. or Canada who hold the M.D. or Ph.D. degree. The fellowships are intended for recent graduates (who as a rule are less than 30 years of age). **Welch Fellowships in Internal Medicine**, also administered for The Rockefeller Foundation, provide a prolonged period of advanced training to persons of proved research ability. They are open to physicians under 40 years of age who are citizens of the U. S. **Fellowships in Tuberculosis** have been made available by a grant from the National Tuberculosis Association. These awards are limited in number and are designed to promote the training and development of investigators in this field. They are open to citizens of the U. S. who are graduates of American schools and preferably not more than 30 years of age. Preference will be given to applicants who have the degree of M.D. or Ph.D. Only in exceptional circumstances will a fellowship be awarded to an applicant without either of these degrees. Fellows will be appointed at a meeting of the Medical Fellowship Board early in

March 1951. Applications for consideration at this meeting must be filed before *December 1, 1950*. Appointment may begin at any date determined by the board. For further information, address the Secretary, Medical Fellowship Board, National Research Council, 2101 Constitution Avenue, N.W., Washington 25, D.C.

## Deaths

**Ewald Boecking**, 56, inventor and mechanical engineer, died at his home in Great Kills, Staten Island, N. Y., August 18. Dr. Boecking was the inventor of a film projector designed to eliminate flicker and to provide a clearer picture on the screen, a major improvement in projection technique.

**Nicholas Mikhailovich Oboukhoff**, 77, research professor emeritus of electrical engineering and professor emeritus of mathematical physics at Oklahoma A & M College, died July 30 in Stillwater, Okla. Dr. Oboukhoff was the author of many scientific and technical papers published in France, Russia, China, Germany, and the U. S.

**James I. Shannon, S.J.**, director of the Department of Physics, Saint Louis University, St. Louis, Mo., since 1913, died September 8, at the age of 81. A member of the faculty from 1909, Father Shannon was active in building up the Department of Physics, and in addition taught field courses in geology.

**Julius Terrass Willard**, chemist, administrator, and college historian of Kansas State College, died July 26, at the age of 88. Dr. Willard had been a member of the faculty since 1883 and had served as dean of general science until 1930, as well as two terms as acting president of the college.

**M. F. Coolbaugh**, 73, president emeritus of the Colorado School of Mines and a nationally known consulting engineer, died September 9 as the result of a heart attack. The new million-dollar Colorado School of Mines chemistry building, now under construction, has been named in his honor.



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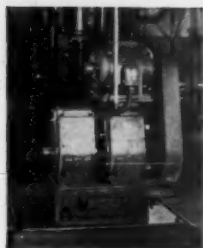
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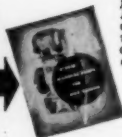
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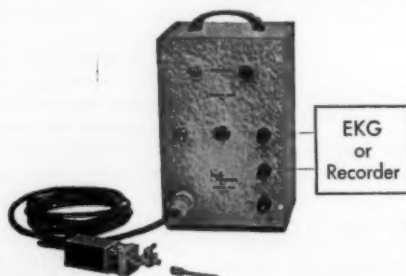
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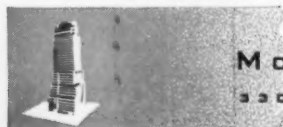
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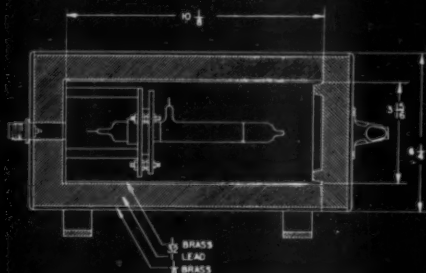


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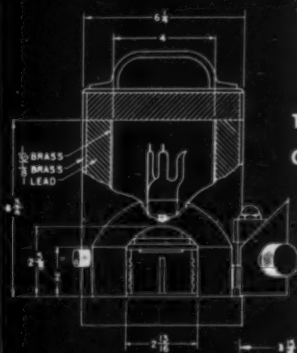
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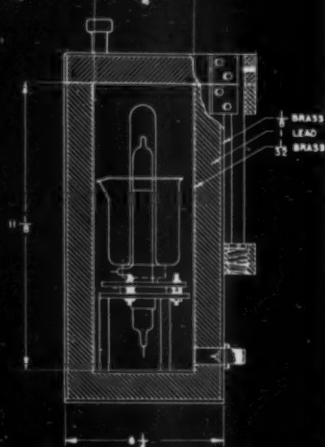


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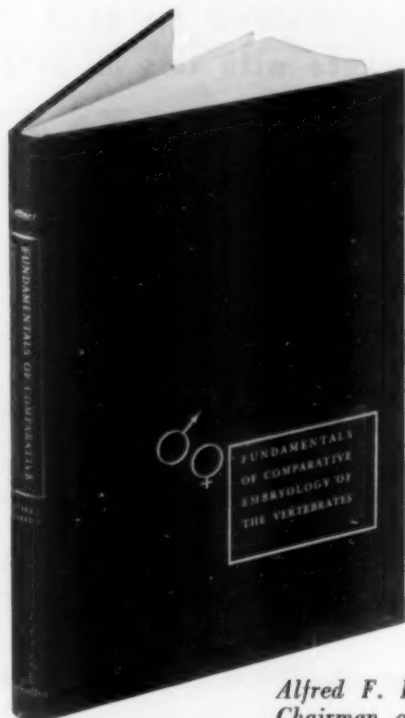
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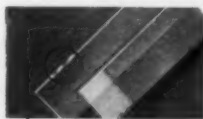
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# HOTEL RESERVATIONS

## 117th AAAS MEETING

Cleveland, December 26-30, 1950

The list of hotels and the reservation coupon below are for your convenience in making your hotel room reservation in Cleveland. Please send your application, *not* to any hotel directly, but to the Housing Bureau of the Cleveland Convention and Visitors' Bureau to avoid delay and confusion. The experienced Housing Bureau will make assignments promptly and the hotel will send a confirmation directly to you in two weeks or less. **Please plan to share a room with a colleague.** In addition to economy, this will insure ample accommodations for all in the *downtown* hotels. Mail your application *now* to secure your first choice of desired accommodations.

### HOTELS AND RATES PER DAY

Hotel*	Single	Double	Twin-Bedded	Suites
STATLER	\$4.00-\$8.00	\$7.00-\$10.00	\$8.50-\$12.50	\$17.00-\$23.00
HOLLENDEN	\$3.50-\$8.00	\$5.50-\$10.00	\$7.00-\$12.00	\$12.00-\$22.00
CARTER	\$4.00-\$6.50	\$6.00-\$10.00	\$7.00-\$10.00	\$18.00-\$25.00
ALLERTON	\$3.50-\$7.00 \$2.50 RW	\$6.00-\$ 9.00	\$6.00-\$10.00 \$4.00 RW	\$10.00-\$20.00
AUDITORIUM	\$3.50-\$5.00	\$5.50-\$ 7.50	\$7.50	\$12.50-\$26.00
OLMSTED	\$3.00-\$6.00	\$5.00-\$ 9.50	\$7.00-\$ 9.50	\$10.00-\$15.00

Prices are subject to change, but are not likely to do so.

RW means running water only—no private bath.

\* A list of the headquarters of each society and section is under **Association Affairs, SCIENCE**, August 25 and in **THE SCIENTIFIC MONTHLY** for September.

### THIS IS YOUR HOTEL RESERVATION COUPON

Mrs. Louise D. Perkins, Director  
Housing Bureau  
Cleveland Convention and Visitors' Bureau, Inc.  
511 Terminal Tower  
Cleveland 13, Ohio

Date of Application .....

Please reserve the following accommodations for the 117th Annual Meeting of the AAAS:

#### TYPE OF ACCOMMODATION DESIRED

Twin-Bedded .....	Rate .....	Number in Party .....
Suite .....	Rate .....	
Double Room .....	Rate .....	
Single Room .....	Rate .....	

..... persons

Sharing this room will be:

(Enumerate and attach list giving name and address of each person, including yourself)

#### CHOICE OF HOTEL

First Choice ..... Second Choice ..... Third Choice .....

DATE OF ARRIVAL ..... DEPARTURE DATE .....

(These must be indicated)

SIGNED .....

(Please print or type)

ADDRESS .....

(Street)

(City and Zone)

(State)

Mail this now to the Housing Bureau.

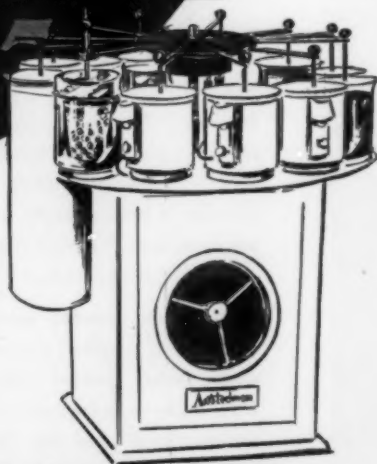
Rooms will be assigned and confirmed in order of receipt of reservation.

Hotels will confirm directly in two weeks or less.

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